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NONSPECIFIC MESENTERIC LYMPHADENITIS

REPORT OF SEVENTY-FIVE CASES

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PITTSBURGH

Mesenteric lymphadenitis is by no means a new pathologic entity. Much has been written about in in recent years. However, as a clinical entity it is unknown or frequently forgotten by a large group of medical men as well as surgeons. I present this article in order to emphasize the fact that this disease occurs in everyday practice, and often just keeping it in mind allows one to explain an otherwise baffling array of symptoms. When one is on the lookout for this disease entity (if I may call it such), one may be rewarded by makin a correct diagnosis, the verification being made at the operating table.

I am especially interested in mesenteric lymphadenitis from the point of view of: (1) diagnosis, which is often obscure; (2) etiology, which is still in doubt, and (3) treatment and prognosis.

My experience and that of authors whose writings have been consulted have led me to use the following clinical classification for this disease: (1) chronic mesenteric lymphadenitis, (2) acute mesenteric lymphadenitis, (3) acute fulminating mesenteric lymphadenitis and (4) acute suppurative mesenteric lymphadenitis.

Before discussing these various forms, I should like to stress the fact that this is not a pathologic classification but a clinical one based on history, physical examination and operative findings.

Under chronic mesenteric lymphadenitis are included cases in which the patient comes to operation for so-called chronic appendicitis. Usually there is chronic recurrent pain in the right lower quadrant, which may be vague in distribution or localized to the right side. The monotony of indefinite abdominal pain may be broken by acute exacerbations, often related to an infection of the upper respiratory tract, acute tonsillitis or cervical adenitis. There may or may not be associated gastro-

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intestinal symptoms—more often they are minimal. The temperature and pulse rate may be slightly elevated, if at all, and the same might well be said of the white cell count. Physical examination will usually show a point of tenderness in the right lower quadrant of the abdomen, with no rigidity. A point has been described slightly above and medial to McBurney's point as a maximum area of tenderness. In my experience this point of maximum tenderness is of variable position, and I think it sufficient to say that there is tenderness in the right lower quadrant.

If the patient is operated on at a time when he is relatively free from symptoms, the appendix will be found to be grossly normal; and if the mesentery is inspected, it will be found studded with enlarged glands in the ileocecal region, the size varying from that of a pea to that of a kidney bean and increasing toward the root of the mesentery.

Anatomists say that glands in the ileocecal region vary from one hundred to one hundred and fifty in number, there being two paths of flow—one toward the mesenteric glands and the other retroperitoneally along the ascending colon. One may voice the objection that it is a fairly normal state of affairs to find enlarged glands in the mesentery. That this is not so is attested to by the fact that any number of times I have inspected the mesentery at various types of laparotomy and have not been able to see or palpate mesenteric glands. Moreover, Mead [1] has shown in a rather exhaustive study of an extensive series of autopsies that mesenteric glands which can be seen and palpated by the examining finger are definitely an abnormal finding.

The usual procedure in this type of case is to remove the appendix, and the usual liberal pathologic report of chronic appendicitis is made. If one of these glands is removed for pathologic section and culture, the examination will show hyperplasia and the culture will be negative. Figure 1 is a photomicrograph of a section taken from one of these glands. The pathologic report as rendered by Dr. K. Yardumian is as follows:

Gross Description: The specimen consists of a lymph node the size of a split pea, fairly firm in consistency. The capsule is intact. It is rather pale gray. On section the capsule is slightly thickened and has a smooth pinkish gray surface.

Microscopic Description: Sections show moderate thickening of the capsule with a slight increase of trabeculae and advanced hyperplasia of the reticulum cells with replacement of areas of lymph tissue by reticulum cells. The sinusoids are filled with endothelial leukocytes. No mitosis is present.

Diagnosis: Chronic toxic lymphadenitis (nonspecific).

The second type, which I have arbitrarily called the acute variety, merges insensibly into the first. There may or may not be an antecedent

1. Mead, Charles: Mesenteric Lymphadenitis Simulating Acute Appendicitis: Quantitative Study of Size of Normal Mesenteric Lymph Nodes, Arch. Surg. **30**:492-527 (March) 1935.

history of acute abdominal pain. The pain may be identical in nature and distribution with that of acute appendicitis. Often, however, it is more colicky, this being explained on a basis of intestinal spasm secondary to irritation in the mesenteric root. The radiation of pain is usually to the right lower quadrant. Nausea is present as a rule, but emesis is not so frequent. The temperature varies from 99 to 101 F., and the pulse is generally accordingly increased. The patient does not appear very ill, but physical examination shows definite tenderness in

Fig. 1.—Microscopic section of a gland removed in a case of chronic mesenteric lymphadenitis.

the right lower abdominal quadrant, with some spasticity. Some rebound tenderness may be present, and peristalsis is usually normal or even somewhat exaggerated. The white cell count is generally elevated, and the polymorphonuclear count varies from 65 to 90 per cent. This is the type of case in which the surgeon is called in consultation and, after going into the history and examining the patient, announces that he does not believe that the patient has acute appendicitis. However, he is unable to rule it out definitely, and a laparotomy may or may not be performed, depending on the surgical principles by which he abides. At

operation the appendix is found to be normal, but the mesentery is studded with swollen glands reaching the size of an almond. Postoperatively, the temperature gradually approaches normal, and convalescence is thereafter usually uneventful. Figure 2 shows the temperature charts in three typical cases of acute mesenteric lymphadenitis.

If a gland is removed for section and culture, the culture will be negative and the gland will show acute hyperplastic changes. A diagnosis of chronic appendicitis is usually made. Figure 3 is a photomicrograph of a section taken from a gland removed in a case of acute mesenteric lymphadenitis. The following report on this section was rendered by Dr. K. Yardumian:

Gross Description: The specimen consists of a lymph node the size of a navy bean. The capsule is intact. It is soft in consistency and hyperemic. On section, it is pinkish gray, with discrete opaque areas.

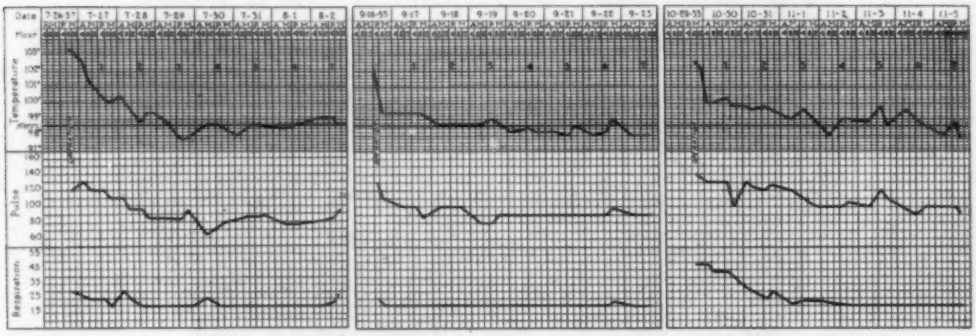

Fig. 2.—Temperature charts in three typical cases of acute mesenteric lymphadenitis.

Microscopic Description: Sections show moderate hyperplasia of the germinal centers with a few mitotic figures and thinning out of the lymphocytic zone. There are dilated capillaries and sinusoids with areas of extravasation of blood and moderate proliferation of the reticulum cells. No polymorphonuclear infiltration is seen, and there is no evidence of a specific inflammatory reaction.

Diagnosis: Acute toxic lymphadenitis (nonspecific).

The third type of mesenteric lymphadenitis, which I have chosen to call acute fulminating mesenteric lymphadenitis, presents a very different picture. It is impossible to differentiate this condition from rapidly advancing acute appendicitis. As a matter of fact, the picture is so overwhelmingly that of an acute abdominal catastrophe that one does not even consider a diagnosis of acute fulminating mesenteric lymphadenitis. The patient is usually a child and presents the picture of an acute toxic state. The story is one of diffuse abdominal pain, generally localizing in the right lower quadrant and associated with

protracted emesis. The face is flushed, breathing is rapid, and the tongue is coated and dry. Examination of the abdomen reveals diffuse tenderness in both the right and the left lower quadrant, with a variable amount of rigidity. Rebound tenderness is usually exquisite, even in the left lower quadrant. Abdominal peristalsis is absent or greatly diminished. The temperature varies from 101 to 103 F., and the pulse is rapid and bounding. The white cell count is high, hovering around 20,000, with a high percentage of polymorphonuclears. All in all, one

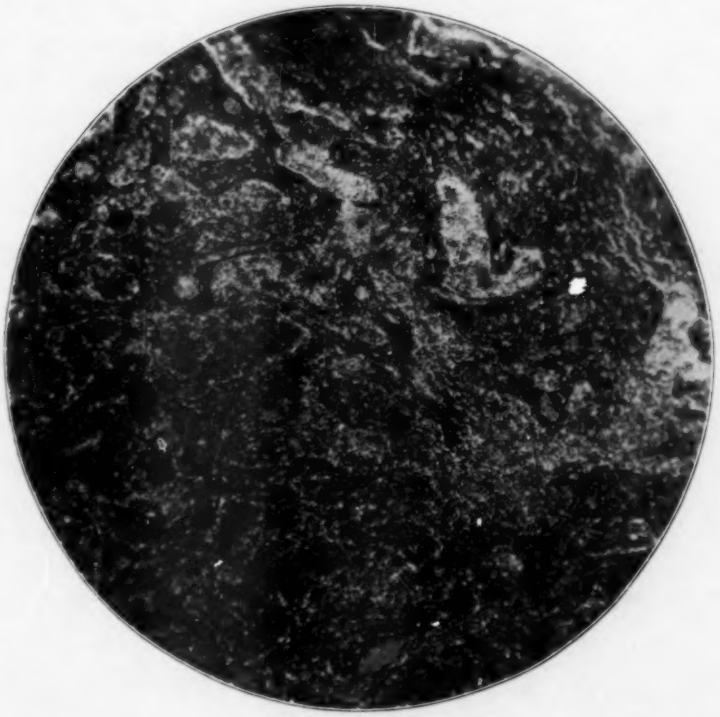

Fig. 3.—Microscopic section of a gland removed in a case of acute mesenteric lymphadenitis.

gives the patient a rather guarded prognosis on the basis that he has acute appendicitis with peritoneal contamination. On opening the abdomen one finds a fair amount of clear to slightly cloudy fluid, accounting no doubt for the pain on the left side. Culture of this fluid will be found to be negative. The small and large intestines, including the appendix, will show diffuse injection. Otherwise, to the surgeon's great surprise, the appendix is practically normal. The mesentery, however, is studded with acutely swollen glands, which give one the impression of wanting literally to pop out of the mesenteric leaves.

Some men have described an exudative process in the peritoneal cavity in connection with the acute process in the mesenteric glands. I have not encountered this type as yet. In one of the cases I found what I have chosen to call acute hemorrhagic mesenteric lymphadenitis. Besides the aforementioned swelling of the glands, I noted diffuse hemorrhages throughout the glands. Postoperatively, the patient with acute fulminating mesenteric lymphadenitis is quite ill for a few days, the temperature gradually seeks normal and convalescence is soon firmly established. Figure 4 is a temperature chart illustrative of this type of case.

It has been my good fortune to date not to encounter the fourth type, namely, acute suppurative mesenteric lymphadenitis. However, in such cases one or more glands go on to suppuration, with resultant

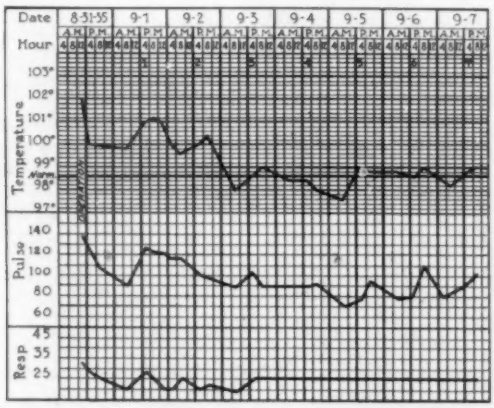

Fig. 4.—Temperature chart in a case of acute fulminating mesenteric lymphadenitis.

spreading peritonitis or abscess formation. Whether this entity is the late result of the other forms which I have described, I am not prepared to state. Suffice it to say that the picture is one of acute peritonitis with resultant diffuse spread or abscess formation. The prognosis in the former is very grave, and that in the latter is more favorable as to ultimate recovery.

DIAGNOSIS

At the beginning of this article I stated that I was especially interested in three phases of this entity.

The first of these is diagnosis. I might go on at length and outline all the various diseases which might be confused with mesenteric lymphadenitis, varying all the way from ureteral calculus to ordinary gastroenteritis. However, practically speaking, the diagnosis of the chronic variety of mesenteric lymphadenitis presents the same problem as the

diagnosis of chronic appendicitis. Involvement of the urinary tract, the pelvic organs and the genito-urinary tract must be ruled out. Then one is confronted with the question of whether the condition is chronic appendicitis or chronic mesenteric lymphadenitis. A history of attacks related to infections of the upper respiratory tract may help in diagnosis. As the criteria for a diagnosis of chronic appendicitis (even in the pathologic laboratory) are rather vague, the question as to whether the appendix or the glands (when found at operation) are at fault still remains in abeyance. Even the problem as to whether the enlarged glands do or do not result from chronic appendicitis must necessarily evade settlement at the present time.

In the acute variety it is the differential diagnosis from acute appendicitis which is of main concern. I am loath to admit that as yet I have been unable to settle on any real practical differentiating point. It is needless to go into detail concerning the various points in the history and physical examination, because I am ultimately left with the following dictum: If one cannot rule out acute appendicitis the abdomen must be opened. I have tried the sedimentation test as a means of differentiation, only to find that it is of no real value in this type of case, the sedimentation time being long in both the ordinary case of acute noncomplicated appendicitis and the ordinary case of acute mesenteric lymphadenitis. Recently, I utilized the Schilling index in the differential diagnosis of the acute abdominal condition, but in my hands it has been of no great value, especially in the dubious case. The only statement I feel justified in making is as follows: When one encounters a patient who presents an atypical picture of acute appendicitis, especially when there is a history of an acute infection of the upper respiratory tract, acute mesenteric lymphadenitis should be kept in mind.

As to the acute fulminating and acute suppurative types, I do not believe it possible even to consider a differential diagnosis.

ETIOLOGY

The etiologic factor in this disease is one on which authorities have not agreed. I have chosen the term nonspecific because I believe that in the great majority of cases I am dealing with a nontuberculous factor. I do not deny that there is such an entity as tuberculous mesenteric lymphadenitis, but it is my opinion that the cases reviewed here are predominantly of a nonspecific variety. In this opinion I am supported by Wilensky,[2] Hahn[3] and others. Some authors have injected excised mesenteric glands into guinea-pigs, with from 20 to 40 per cent positive

2. Wilensky, A. O.: M. Rec. **98**:770 (Nov. 6) 1920.

3. Wilensky, A. O., and Hahn, L. J.: Ann. Surg. **83**:812-826 (June) 1926.

results for tubercle bacilli. These studies form the basis for the belief which one school holds that mesenteric lymphadenitis is tuberculous in the greatest percentage of cases.

The difficulty in proving the etiologic factor lies in the facts that these cases are usually not fatal and that surgeons are loath to (and rightly so) remove a mesenteric gland because of danger to important intestinal vessels in the mesentery. However, some men have removed glands for study. The results of microscopic section in my series of six glands have failed to show any histologic evidence of tubercle formation. Inoculation of guinea-pigs was not carried out because of insufficient material.

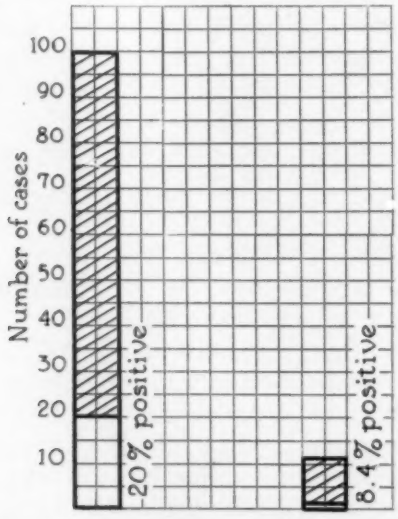

Fig. 5.—Chart showing the results of tuberculin tests in one hundred routine cases and twelve cases of mesenteric lymphadenitis.

In an attempt to disprove the tuberculous etiology, I thought that a comparison of the results of tuberculin tests in a series of cases of mesenteric lymphadenitis with those in a series of routine cases observed at the hospital might be of value. It is my conception that if mesenteric lymphadenitis does have a tuberculous basis one could certainly expect a much higher percentage of positive reactions in the former series of cases than in the latter. The following has been my experience: In a series of twelve cases of mesenteric lymphadenitis, one positive tuberculin reaction was obtained, giving a percentage of about 8.4 per cent. In a series of one hundred routine cases, sixty of which were cases of abdominal conditions, there were twenty positive reactions, or 20 per cent. Figure 5 shows these results.

I fully realize that the series is small, perhaps too small, to permit drawing of conclusions. However, there is no mistaking the fact that in the series of cases of mesenteric lymphadenitis there was even a lower percentage of positive tuberculin reactions than in the series of ordinary cases in which tuberculosis was not suspected. I feel certain that if one performed tuberculin tests in a series of twelve cases of tuberculous cervical adenitis, a high percentage of positive reactions would be obtained. I see no reason why the same should not be true of mesenteric lymphadenitis, assuming that it were on a tuberculous basis.

If the tubercle bacillus is not the etiologic factor, where may one look further for the cause? Goldberg and Nathanson [4] cultured material from the throat in a series of these cases and obtained Streptococcus haemolyticus. Cultures from the glands removed for biopsy showed the same organism in one of eight cases.

In my series of six glands aerobic cultures were performed, and I was unable to obtain growths from any. Anaerobic cultures were run on three of these because I felt that perhaps the organism being possibly

TABLE 1.—*Results of Laboratory Investigation*

Number of glands removed for biopsy	6
Evidence of tuberculosis	None
Number of glands removed for culture	6
Aerobic culture (sterile)	6
Anaerobic culture (sterile)	3

absorbed in the gastro-intestinal tract was anaerobic. However, no positive cultures were obtained.

It is logical to look for the cause in the intestinal tract. I have not been able to demonstrate any lesion, at least from the serosal side. Some authors have visualized a catarrhal enteritis or minute ulceration as the point of entrance for micro-organisms. However, the paucity of gastro-intestinal symptoms militates against this assumption. Moreover, in the one fatal case in this series autopsy failed to show any gross evidence of intestinal lesions. I do not feel that the appendix is at fault (although proof of this assumption is not available), because I view with suspicion the diagnosis of chronic appendicitis which is so liberally returned by the pathologist. It might be of interest to state at this point that only rarely in cases of acute appendicitis does one see enlarged mesenteric glands.

It is an established fact that one often sees acute abdominal pain associated with acute tonsillitis and infection of the upper respiratory tract.[5] It is fairly well accepted that this pain is probably on a mesen-

4. Goldberg, S. L., and Nathanson, I. T.: Am. J. Surg. **25**:35-40 (July) 1934.

5. Brennemann, J.: "Abdominal Pain of Throat Infections in Children," and Appendicitis, J. A. M. A. **89**:2183-2186 (Dec. 24) 1927; Abdominal Pain of Throat Infections, Am. J. Dis. Child. **22**:493-499 (Nov.) 1921.

teric lymphadenopathic basis. How can this spread be explained? One must assume either that it is due to toxic infective products reaching the ileocecal junction and then being absorbed or perhaps that it is spread by the hematogenous route.

Within the past few years a well known epidemic of meningoencephalitis occurred at Windber, Pa. According to reports obtained from Dr. H. Schlesinger,[6] the onset was marked by a red granular throat, and a large percentage of the children complained of pain in the right lower abdominal quadrant, which eventually disappeared. The infective agent here was no doubt a virus, and I am of the opinion that investigation of these glands along this line might possibly disclose a

TABLE 2.—*Clinical Observations in Seventy-Five Cases of Mesenteric Lymphadenitis*

	Types of Disease			
	Chronic	Acute	Acute Fulminating	Suppurative
Number	35	38	2	0
Percentage	47	50	3	0

	Sex of Patients	
	Male	Female
Number	20	55
Percentage	26	74

Acute foci of infection	Number of Cases (as Noted on Charts)
Tonsillitis	5
Carious teeth	1
Coryza	2
Cervical adenitis	1
Pharyngitis	1
Suppurative focus in arm	1

virus as the infective agent. It might well explain the negative cultures and the pathologic pictures.

From a series of seventy-five cases of mesenteric lymphadenitis, including instances of the chronic, the acute and the acute fulminating form, in which operation was performed at this hospital during the past six years, I have made various observations. Table 2 shows that the acute forms were slightly in the majority. The tabulation of the cases as to sex showed preponderance of females, almost 3 to 1. The presence of an acute focus of infection was noted in only eleven cases.

It is the commonly accepted impression that this disease occurs most frequently in young children. I have no doubt that a great many children as well as adults with mesenteric lymphadenitis are not operated on. In these there is no absolute proof of the diagnosis. However, a

6. Schlesinger, H.: Personal communication to the author.

tabulation of the seventy-five cases in which operation was performed and glands demonstrated shows the greatest incidence of the disease to be in persons between the ages of 13 and 20. There were no patients operated on below the age of 5, and the minimal number of cases was found in persons between the ages of 5 and 12. Figure 6 shows the results in this age tabulation.

Further study reveals a definite seasonal incidence for this entity. Figure 7 shows the greatest number of cases to have occurred in the

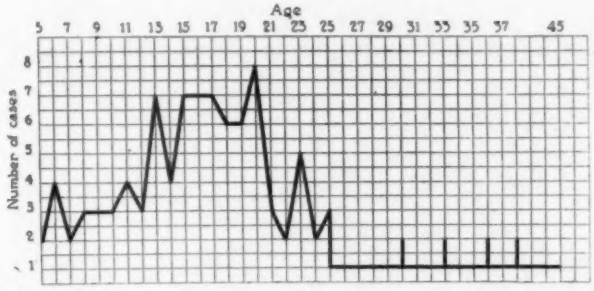

Fig. 6.—Chart showing the age at which mesenteric lymphadenitis occurred.

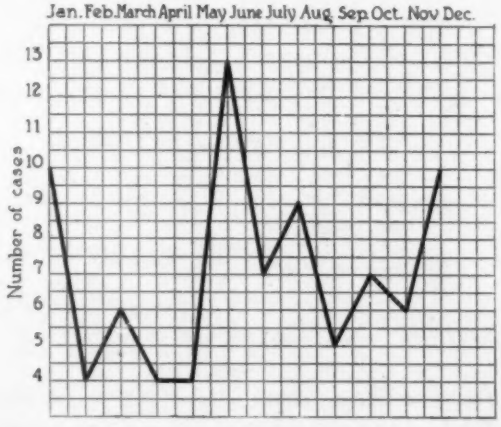

Fig. 7.—Chart showing the seasonal incidence of mesenteric lymphadenitis.

months of June to August inclusive and in October to January inclusive. The least number of cases occurred in the period between February and May.

It has been claimed, and perhaps rightly so, that the tonsils are a portal of entry in this disease. I thought that it might be interesting to investigate whether the tonsils and adenoids had been removed previous to laparotomy in these seventy-five cases. I found that twenty-three, or about 30 per cent, of the patients had had their tonsils

and adenoids removed. The records stated that they were present in nine. There was no note as to their presence in the remaining forty-three patients. I think it fair to assume that in at least from 15 to 20 per cent of the latter patients the tonsils and adenoids had probably been removed. I state these facts merely to show that the tonsils and adenoids cannot be the offending factor in cases in which they had been previously enucleated. However, I do agree that the remaining lymphatic tissue in the throat or perhaps the teeth could well act as the offending focus.

TREATMENT

Treatment at present is supposedly purely operative, it being assumed that laparotomy in itself results in relief from future pain.

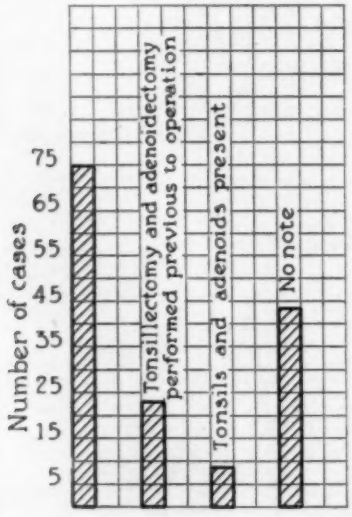

Fig. 8.—Chart showing the results of an investigation as to the presence or absence of tonsils or adenoids in the seventy-five cases of mesenteric lymphadenitis.

Perhaps this is where the impression arises that the etiologic factor is tuberculous, as tuberculous peritonitis is supposed to respond to simple laparotomy. I was not satisfied that laparotomy could result in such a dramatic and permanent cure. Follow-up letters were therefore sent out to the seventy-five patients who were proved to have mesenteric lymphadenitis. These letters were simply phrased as to the presence or absence of abdominal pain and as to the type of abdominal pain which the patient experienced. Replies were received from twenty-nine persons. Of these twenty-nine, ten replied that they had no pain. Ten replied that they had pain similar to their preoperative complaint. The remaining nine still had abdominal pain, but not identical with the pain for which they had been operated on. In other words, nineteen

of twenty-nine, or roughly two thirds, of these patients who replied to the inquiries still had abdominal pain of one type or another. This type of follow-up study is not entirely satisfactory in that the last nine patients might well be having pain from abdominal adhesions or some other abdominal factor, but certainly one can get the impression that laparotomy is not the cure-all for these patients' symptoms. I believe that postoperative supportive measures and convalescent care are probably more responsible for relief of symptoms than the simple laparotomy. I think that the liberal use of cod liver oil and ultraviolet radiation and the eradication of foci might well be an important factor in the alleviation of symptoms. At this point, I should like to suggest

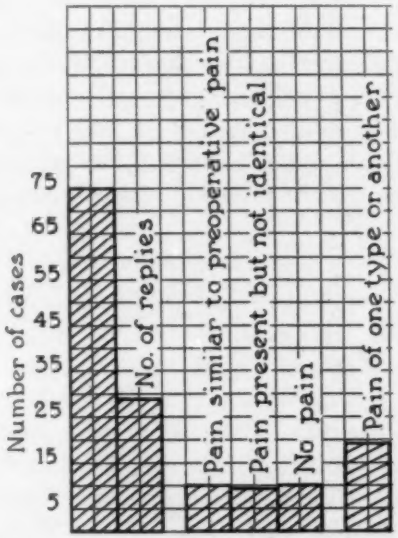

Fig. 9.—Chart showing the results of a follow-up study as to the presence or absence of pain in twenty-nine cases of mesenteric lymphadenitis.

that roentgen therapy for those persons with persistent symptoms might be worth a trial on the same basis that roentgen therapy is given for cervical adenopathy.[7]

Figure 9 shows the results of follow-up letters as to abdominal pain.

SUMMARY

Nonspecific mesenteric lymphadenitis can be divided into four types, clinically: (1) chronic, (2) acute, (3) acute fulminating and (4) acute suppurative.

7. Bell, L. P.: Surg., Gynec. & Obst. **45**:465-473 (Oct.) 1927.

Diagnosis of the chronic type resolves itself into an elimination of other causes of the presenting symptoms. The acute variety is often confused with acute appendicitis, and operation is usually required to decide the issue.

The following conclusions were made concerning the etiology:

(*a*) Tuberculin tests indicated that the tubercle bacillus is not the offending organism.

(*b*) Cultures and sections in six glands failed to show evidence of pyogenic or tuberculous infection.

(*c*) There is a definite seasonal incidence, perhaps related to infection of the upper respiratory tract.

(*d*) Foci of infection are probably important etiologic factors. In twenty-three of seventy-five cases reviewed the patients had undergone tonsillectomy and adenoidectomy previous to operation, thus eliminating the tonsils and adenoids as a source of infection in these cases.

In a series of twenty-nine replies to follow-up letters, two thirds of the patients still had abdominal pain after laparotomy. Postoperative supportive measures are probably of great value in the alleviation of symptoms.

CONCLUSION

In conclusion, I should like to say that nonspecific mesenteric lymphadenitis is a definite entity which can be diagnosed with greater frequency if looked for and kept in mind. I feel that the etiologic factor has yet to be found. Whether the infective agent simultaneously attacks the lymphatic tissue of the respiratory tract and abdomen or secondarily attacks the abdomen with the nose and throat as a focus, it is my impression that focal infection is a more important part of this picture than any theoretical enteric lesion.

I hold no brief against tuberculous mesenteric lymphadenitis, but I feel that the condition seen so frequently at the operating table is in a large percentage of cases of nonspecific origin and should not be laid at the door of the tubercle bacillus.

Dr. Landon, Dr. Schubb and Dr. Frankenstein permitted me to use their records.

SCIATIC SCOLIOSIS

A CLINICAL ANALYSIS OF EIGHTY CASES

MAX A. LEVINE, M.D.
LOS ANGELES

The purpose of this paper is to present the clinical manifestations and results following a uniform type of treatment in the not infrequent complication of pain low in the back, termed "sciatic scoliosis." The theoretical considerations have been thoroughly discussed in another clinical study by Kleinberg.[1]

Briefly, in cases of sciatic scoliosis one has to deal with a lateral curvature of the spine, which most frequently is the result of a derangement (arthritis, sprain, etc.) of the sacro-iliac or sacrolumbar joints, with gluteal myositis or with sciatic neuralgia (sciatic perineuritis). These conditions give rise to pain, which is transmitted along the course of the sciatic nerve. In an attempt to recede from the painful side or area, the patient will unknowingly tilt his trunk laterally and most frequently away from the affected side, producing a functional type of scoliosis. As will be observed later, this is not a true structural scoliosis because of the lack of fixed torsion of the vertebral bodies.

ANALYSIS OF DATA

In the analysis of the etiologic data in eighty cases of sciatic scoliosis it was noted that approximately two thirds of the patients were in the fourth and fifth decades; that there was a conspicuous absence of persons in the first decade, and only an occasional patient in the second, sixth and seventh decades (table 1). The frequency as to sexes was 3:1, the males predominating. Occupations were varied. Among the males, salesmen, printers and chauffeurs were most frequently affected, while among the females, housewives predominated. There was a noteworthy infrequency of the condition among those who did hard labor, possibly because the exercise attendant on their work led to better muscular development. Severe trauma was a predisposing factor in approximately one third of the cases, while mild trauma was contributory in about one eighth. As has been noted previously,[1] infection of

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Orthopedic Service of Dr. Samuel Kleinberg.

From the Hospital for Joint Diseases, New York.

1. Kleinberg, S.: Sciatic Scoliosis Due to Low Backache, Am. J. Surg. **7**: 89-94, 1929.

the upper respiratory tract will not infrequently predispose to this condition, as it was the factor in one eighth of the cases.

Backache due to derangement of the sacro-iliac or lumbosacral joints, which was the exciting cause in the irritation of the sciatic root, came on abruptly in over two thirds of the patients, and in the remaining one third there was an insidious onset. About one third of the patients gave a history of recurrent pains in the back, while the remaining two thirds were affected for the first time. These attacks occurred intermittently for from four days to twenty years.

TABLE 1.—*Etiologic Data in Eighty Cases of Sciatic Scoliosis*

	Cases	Percentage
Number of patients according to decades (age 16-65, average 35.)		
First	0	
Second	6	7.6
Third	12	15.2
Fourth	33	42.3
Fifth	20	25.6
Sixth	6	7.6
Seventh	1	1.1
Unmentioned	2 adults	
Sex		
Males	62	77.5
Females	18	22.5
Occupations		
Males: salesmen, printers, chauffeurs, merchants, students, painters, brokers, pressers, pedlers, bookkeepers, laborers, helper, awningmaker, silk manufacturer, iron worker, caretaker, janitor, advertising man, iceman, plumber, pharmacist, shipping clerk, floorer, butcher, knitter, neckwear operator, office worker, rabbi, physician, unmentioned (8)		
Females: housewives, students, nursemaid, hairdresser, school teacher, saleslady, nurse, dress operator, unmentioned (4)		
Trauma		
Mild	7	8.7
Severe	20	32.5
Illness		
Infection of the upper respiratory tract	6	7.5
Exposure to cold weather	2	2.4
"Arthritis"	1	1.2
Onset		
Insidious	25	32.0
Abrupt	53	68.0
Unknown	2	2.4
Backache		
1. Primary attacks (duration, 14.6 mo.)	53	66.3
2. Recurrent attacks (duration, 18.6 mo.)	27	33.7

An analysis of the symptomatology in these cases of sciatic scoliosis affords some interesting observations (table 2). The characteristic gait was a prominent feature. The greatest number of patients walked with the trunk stooped forward, flexion being either at the hip or at the sacrolumbar joints. Quite frequently the gait signs were combined in the same person, as the trunk forward (flexed) and guarded and an awkward gait.

Almost one third of the patients complained of generalized pain low in the back, while approximately one fourth indicated the sacro-iliac joints. Also, one fourth of the patients had pain over the buttock, which

TABLE 2.—*Symptomatology in Eighty Cases of Sciatic Scoliosis*

	Cases	Percentage
Gait		
Limp	13	16.0
Awkward	12	15.0
Guarded	6	7.5
Stooped forward	20	25.0
Unknown	29	31.5
Pain		
1. Location		
Sacro-iliac region	18	22.0
Lumbosacral region	1	1.2
Buttock	20	25.0
Lower part of back	29	31.5
Hip	10	12.0
Thigh	44	55.0
Leg	42	52.0
Foot	17	21.0
2. Sides		
Right	34	42.0
Left	41	51.0
Middle of back	5	7.0
Deformity of the back		
1. Standing position		
Tilt of trunk to the affected (painful) side*	25	33.0
Tilt of trunk to the well (painless) side†	48	63.0
Tilt of trunk alternating to the well, then affected side and (vice versa)	3	4.0
2. Prone position		
Disappearance of tilt	25	33.0
3. Physiologic curves		
A. Flatness or diminution of the normal curves		
a. Lumbar lordosis	34	51.0
b. Dorsal kyphosis	14	21.0
B. Complete reversal of the normal curves	11	16.0
C. Exaggeration of the normal curves		
a. Lumbar lordosis	4	5.9
b. Dorsal kyphosis	3	4.1
Mobility of the spine: 1. Restricted		
Flexion	63	78.0
Extension	52	65.0
Hyperextension	16	20.0
Lateral inclination	60	75.0
Muscle spasm	25	33.0
Tenderness		
Sacro-iliac region	41	51.0
Sciatic nerve		
Sacrosciatic notch	8	10.0
Thigh	19	23.0
Leg	14	17.0
Lumbosacral region	4	5.9
Gluteal region	11	16.0
Ilium	3	4.0
Lumbar muscle	7	10.5
None present	10	12.0
Straight leg raising		
1. Restricted,‡ (a) with pain in		
Left buttock	9	11.0
Left thigh	8	10.0
Left leg	3	4.0
Left sacro-iliac region	15	18.0
Left lumbosacral region	3	4.0
Right buttock	5	6.0
Right thigh	7	10.0
Right leg	2	2.5
Right sacro-iliac region	9	11.0
Right lumbosacral region	1	1.2
2. Unrestricted		
Left	12	15.0
Right	13	16.0
Neurologic signs		
1. Reflexes: absent or diminished on the affected side		
a. Patellar	4	5.9
b. Achilles	19	24.0
2. Sensory changes: hypalgesia		
a. Thigh	1	1.2
b. Leg	1	1.2
c. Foot	3	4.1
3. Atrophy		
Thigh	12	15.0
Leg	5	6.2
Buttock	3	4.1
Roentgen examination (41 cases) of pelvis and lumbar portion of spine		
1. Clinically affected side		
Haziness of the sacro-iliac joints (arthritic changes)	16	40.0
Arthritis of the lumbar portion of spine	9	22.0
Lumbosacral arthritis	2	5.0
Sacralization of the fifth lumbar vertebra	3	8.0
Negative	11	32.0

* This was the side on which the pathologic process was present, viz., a derangement of that sacro-iliac joint.

† This was the side on which the pathologic process was absent.

‡ In many cases both the left and the right leg were restricted.

was usually most exquisite at the level of the sacrosciatic notch. Characteristic pain in the thigh (posterior aspect) and leg (lateral aspect) was present in over one half of the patients, and either one or both types of pain were associated with sensitivity low in the back or in the buttock.

In reviewing the deformity of the back with the patient in a standing position, it was interesting to find that almost two thirds of them tilted the trunk away from (dorsolumbar curve) the painful or affected side, whereas in one third the trunk was tilted to the painful side. In a small percentage (4 per cent) the tilt of the trunk alternated on successive examinations to the well and then to the afflicted side and vice versa. As brought out previously in criteria of structural versus functional scoliosis, with the patients in the prone position, one third of the deformities of the back disappeared prior to treatment, thus proving the functional status of the condition.

Associated with the tilt of the trunk were alterations in the normal physiologic curves. One half of the patients showed a flattening or diminution of the lumbar curves, and approximately one fifth revealed a flattening or absence of the dorsal kyphosis. Complete reversal of the normal curves, e. g., a lumbar kyphosis and a dorsal lordosis, was present in one sixth of the patients. In a relatively small percentage both of the normal curves were exaggerated.

The mobility of the spine was greatly affected. Approximately three fourths of all the spines were restricted in flexion, extension and lateral inclination. It was not unusual to find the various component motions associatively restricted. Also, muscle spasm could actually be observed in a third of the patients. On the foregoing basis, the awkward guarded gait which these patients presented was not an unexpected consequence of their disturbed muscle balance.

Sensitivity to pressure was found to be in the sacro-iliac joints in over half of the cases. Tenderness along the course of the sciatic nerve, from the sacrosciatic notch to the foot, was noted in about 60 per cent. The gluteal region was tender in one sixth of the cases. Tenderness prevailed in other areas but to a lesser extent.

Straight leg raising was restricted in the majority of the patients and was frequently associated with pain in one or the other sacro-iliac or lumbosacral joints or along the course of the sciatic nerve. Not infrequently, raising of the left and right legs was limited in the same person. Only in approximately one sixth of the patients was straight leg raising unrestricted.

The most striking neurologic sign was the absence of the achilles tendon reflex in one fourth of the patients on the affected (painful) side. Even after a result which was considered otherwise successful,

it was not unusual to find that the achilles tendon reflex remained absent. Surprisingly few patients exhibited any hypalgesia, whereas atrophy of the thigh, leg and buttock was not infrequently found. This condition, no doubt, was of neurotrophic origin.

TABLE 3.—*Diagnosis of Sciatic Scoliosis Based on Etiology in Seventy-Seven Cases*

	Derangement of the Sacro-Iliac Joint		Derangement of the Lumbosacral Joint	Periarthritis of the Lumbar Region of the Spine	Perineuritis of the Sciatic Nerve	Sciatica			
						Primary*		Secondary†	
	Left	Right				Left	Right	Left	Right
Left sciatic scoliosis Secondary to.....	8 cases (10%)	8 cases (10%)	3 cases (4%)	1 case (1.2%)	1 case (1.2%)	3 cases (4%)	3 cases (4%)	8 cases (10%)	3 cases (4%)
Right sciatic scoliosis Secondary to.....	14 cases (21%)	11 cases (16%)	3 cases (4%)	.....	.....	2 cases (2.5%)	1 case (1.2%)	3 cases (4%)	3 cases (4%)
Alternating (right and left) scoliosis Secondary to.....	1 case (1.2%)	1 case (1.2%)	.....	.....	.....	1 case (1.2%)			

* Due to a pathologic condition of the nerve, e. g., perineuritis of the sciatic nerve.
† Sciatica accompanying joint derangement and other extramural factors.

TABLE 4.—*Schematic Analysis*

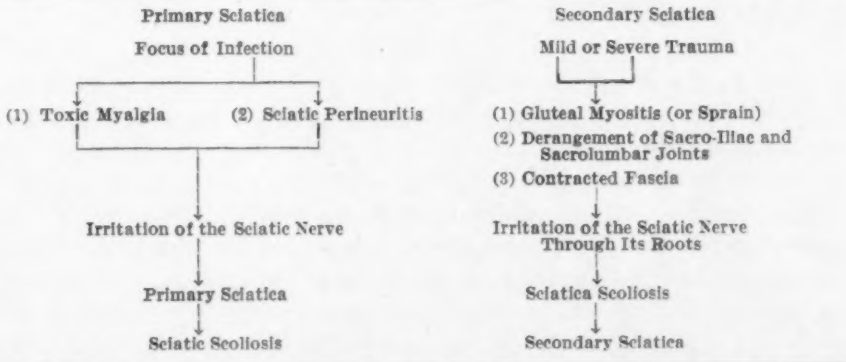

TABLE 5.—*Types of Treatment Used in Sixty-Four Cases*

1. Manipulation of the spine, stretching of involved limb under general anesthesia and application of plaster of paris spica bandage	Traction followed by application of plaster spica	Application of plaster of paris spica under anesthesia; no stretching	Stretching followed by stripping of the gluteus medius muscle; application of plaster spica	1. Injection of sciatic nerve (procaine hydrochloride) 2. Stretching 3. Application of plaster spica	1. Caudal block (a) With stretching (b) Without stretching	Rest in bed
2. Knight spinal brace						
47 cases (73.5%)	2 cases (3.1%)	6 cases (9.2%)	3 cases (4.8%)	3 cases (4.8%)	1 case (1.5%)	2 cases (3.1%)

In reviewing the roentgenograms of the patients suffering from this condition, it was noted that a number did not show any pathologic process (one third). A larger number, however, revealed definite evidences of arthritic changes in the sacro-iliac joints and the lumbar region of the spine (two fifths).

The diagnosis of sciatic scoliosis was based on the exciting etiology. Sciatic scoliosis was practically as frequent on the left as on the right, and the infrequent alternating scoliosis was present in the remainder of the cases (3.8 per cent). Derangement of the joints low in the back was the most frequent exciting cause.

Primary sciatica followed inflammatory changes about the sciatic nerve proper, without involvement of the articulations low in the back. Either perineuritis or toxic myalgia, which was not uncommon after some infection of the upper respiratory tract, may have been the causative agent. In approximately one fifth of the eighty cases the sciatica was classified as primary. In these cases a typical diagnosis was stated as "left sciatic scoliosis, secondary to a right sciatica." Secondary sciatica, on the other hand, was found in those cases in which the exciting causes were derangement of the joints low in the back and gluteal myositides. In about one third of the eighty cases the sciatica was of this type. In this group a typical diagnosis was stated as "left sciatic scoliosis secondary to a derangement of the right sacro-iliac joint and a secondary right sciatica."

TREATMENT

The treatment, which was dependent on the severity of the condition, resolved itself in a uniform set of procedures. In the cases of mild involvement, those in which the sciatic pain was only moderate or mild, the treatment consisted of rest in bed, caudal blocks, injections into the sciatic nerve (at the sacrosciatic notch), unbalanced traction or the application of plaster of paris spica jackets. In the cases of severe involvement, in the majority of which hospitalization was necessary, the technic as followed by Kleinberg [1] was used. The patient was placed on a Hawley table and completely anesthetized; the spine was then manipulated by passive flexion, lateral inclination and hyperextension. The involved extremity, with the knee extended to 180 degrees was flexed at the hip so that the foot was within 15 to 20 inches (38 to 50.8 cm.) of the patient's face, the distance being dependent on the status of the elasticity of the tissues. The involved as well as the uninvolved limbs were brought into hyperextension, thus reforming the physiologic dorsal and lumbar curves. Plaster of paris was applied to the torso, and after it set the involved limb was brought anterior to 180 degrees at the hip. The plaster was then continued to include the toes. The patient was left in this plaster bandage for three

weeks, after which time a Knight spinal brace was applied, and physical therapy in the form of baking and massage was instituted. After six weeks the patient was allowed out of bed and gradually permitted to walk.

Because of tenseness of the gluteus medius muscle and the adjacent fascia, in addition to the stretching procedure as described, the muscle was stripped from its iliac attachments in three cases.

The results were most gratifying after the stretching procedure. In only two instances was a second stretching necessary in order to obtain a satisfactory result. The follow-up period in these cases varied from a few months to five years.

COMMENT

This paper is limited to a discussion of pain low in the back due to derangements of the sacro-iliac and lumbosacral joints and to myositides of the gluteal muscles and primary sciatica. Such lesions as tumors of the spinal cord and involvement of the urogenital tract were not considered, although it is appreciated that they can produce symptoms which may simulate those of sciatic scoliosis.

SUMMARY

Sciatic scoliosis is a clinical syndrome characterized by: lateral curvature of the spine, not infrequent pains low in the back, an awkward guarded gait with a limp, restricted mobility of the spine, tenderness of the joints low in the back and along the course of the sciatic nerve, restricted straight leg raising, not infrequent absence of the achilles tendon reflex on the affected side and relatively few roentgenographic changes.

Eighty patients were studied, sixty-four of whom were treated. The condition in three fourths of these was of the severe type; therefore the stretching procedure and plaster spica bandages were used.

The results were uniformly very satisfactory.

MULTIPLE PERIPHERAL ANEURYSMS ASSOCIATED WITH NONSYPHILITIC DEGENERATION OF THE TUNICA MEDIA

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While multiple small aneurysms of the cerebral and of the pulmonary vessels have been discovered at necropsy, and multiple aneurysms of various of the individual intra-abdominal arterial trunks have been found at operation and at postmortem examination, but relatively few cases of multiple peripheral aneurysms have been reported. Among these may be mentioned the cases of Monro,[1] Kolodny,[2] Aloi,[3] Wilbur,[4] Lemonnier and Bouysset[5] and Leriche and Jung.[6] However, only in the case reported by Aloi, in which aneurysms developed in both popliteal spaces, were all the aneurysms treated surgically.

We wish, therefore, to present a clinical and a pathologic study of a remarkable case, one in which there were at least five major peripheral aneurysms involving the left femoral, right femoral, right popliteal, right subclavian and left axillary arteries; while the aorta and its primary branches were also the seat of the disease which we believe was responsible for the development of the peripheral aneurysms, they were free from any dilatation. The case was further remarkable for the fact that in the process of the surgical treatment of the aneurysms all the major branches of the aorta leading to the head and extremities, except the left carotid artery, were successively ligated without the

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1. Monro, D., in Erichsen, J. E.: Observations on Aneurysm, London, Sydenham Society, 1844, pp. 130-132.

2. Kolodny, A.: Multiple Aneurysms of Large Vessels: Report of a Case, J. A. M. A. **86**:397 (Feb. 6) 1926.

3. Aloi, V.: Un caso di aneurisma multiplo, Ann. ital. di chir. **6**:1121, 1927.

4. Wilbur, D. L.: Multiple Aneurysms of the Arteries of the Right Arm Associated with Arteriovenous Fistula and Arterial Embolism: Report of Case, Am. J. M. Sc. **180**:221, 1930.

5. Lemonnier and Bouysset, C.: Anévrysmes multiples des membres inférieurs dont un avec rupture, Lyon chir. **30**:287, 1933.

6. Leriche, R., and Jung, A.: Neuf anévrysmes latents de la fémorale, de la poplitée et de ses branches. Gangrène de l'avant-pied avec crises vaso-constrictives, Lyon chir. **31**:182, 1934.

production of circulatory deficiency in the brain or in any of the extremities and without any clinical evidence of cardiac embarrassment.

REPORT OF A CASE

History.—A 52 year old Italian-Swiss musician was first admitted to the New York Hospital on Oct. 14, 1932, complaining of "throbbing lumps" on his body. His family history was unimportant, all the members having lived to old age. His past history was significant, however, in several features: He had had diphtheria as a child, with the development of a cervical abscess, which required incision. He also underwent an operation for hernia as a child, which was followed by a recurrence at the age of 20. At 30 an umbilical hernia developed, and this and the recurrent inguinal hernia were successfully repaired the following year. In 1913, at the age of 33, he suffered from "blood poisoning" after stepping on a nail. The local abscess in his foot was incised and drained for two months. In 1921 acute appendicitis developed with peritonitis, for which he was operated on; he remained in the hospital for two months, during which time the wound drained.

There was no history of chancre or of any rash or other type of lesion which might be interpreted as secondary or tertiary syphilis. All Wassermann tests had been negative. In 1931 the patient had some ulcers on his left leg, which healed after the application of an elastic bandage.

The first symptoms referable to the illness under discussion occurred in January 1931, when the patient first noticed a small pulsating lump in the right popliteal space about 4 by 4 cm. in size. This remained about the same size and was painless until January 1932, when it became larger and painful. It then became intermittently painful, causing shooting pains up to the hip and down the back of the leg, with some numbness of the toes and sole of the right foot. In September 1931, pain developed in the right shoulder and arm with numbness of the ring and little fingers of the right hand, and subsequently the patient noted a small, throbbing, painful mass in the right supraclavicular region.

In June 1932 he noted a similar but smaller pulsating mass beneath the outer end of the left clavicle, which caused local pain and was associated with numbness and pain radiating down the left arm to the fingers. About the same time he discovered a small pulsating tumor, 2 by 3 cm. in size, in the left groin, which increased rapidly in size until, at the time of his first admission to the New York Hospital, it was 10 cm. in diameter and caused pain locally.

Finally, in September 1932 a fifth pulsating mass was recognized in the right groin, which was about 6 by 6 cm. in size and was also painful, and which, like all the other masses, caused more pain when the patient was up and about.

Examinations.—On the patient's first admission to the hospital physical examination revealed a fairly well nourished man of about the stated age who had difficulty in walking. The head and neck were normal, except for the presence of a scar about 6 cm. in length on the right side of the neck, evidently the site of incision of the cervical abscess. The chest was well developed, its expansion was normal and there were no evident bony deformities.

At the base of the neck on the right, occupying the mesial portion of the supraclavicular fossa, was a pulsating mass, 6 by 6 cm. in size, over which a systolic thrill could be felt. Auscultation of the mass revealed a bruit synchronous with the cardiac systole. Pressure over this swelling obliterated the right radial pulse.

The heart was apparently normal in size, rhythm and rate. A soft systolic murmur could be heard over the base of the heart up to the neck, which was

thought to be transmitted from the aneurysm. The lungs were clear throughout, and there was no evidence of widening of the area of mediastinal dulness.

The abdomen was slightly protuberant, and its wall was soft and relaxed. A large ventral hernia was present in the right lower quadrant, and here the abdominal wall was thin and contained a large defect. A transverse linear scar 16 cm. in length was evident at the level of the umbilicus. The liver and spleen were not felt, and no masses, tenderness or bruit could be made out in the abdomen. The genitalia were normal, and rectal examination revealed nothing abnormal.

In the left groin and extending downward to the apex of Scarpa's triangle was a swelling, 12 by 12 cm., with an expansile pulsation. A soft systolic bruit was audible over this, and firm pressure on it obliterated the pulsation in the left dorsalis pedis artery.

A smaller pulsating mass, 6 by 8 cm., was evident in the right groin below Poupart's ligament, and over this also a systolic bruit could be heard. A fifth and similar mass, 8 by 12 cm. in size, was to be seen in the right popliteal space. Pressure over this caused the pulsation in the right dorsalis pedis artery to disappear.

Neurologic examination revealed paresthesia over the distribution of the antebrachial cutaneous nerves of the forearms and numbness in the ulnar distribution in the hands. The left leg was normal, but there was definite paresthesia over the lateral aspect of the right foot extending out on the fourth and fifth toes. An area of numbness was present over the arch of the right foot.

The laboratory findings at the time of this admission were unremarkable. The Wassermann and Klein tests of both the patient and his wife were negative. The spinal fluid was negative, and the colloidal gold curve was normal. A blood culture was also negative.

Course.—After the patient's discharge from the hospital on December 14, the aneurysms increased in size and caused considerable pain. The paralysis of the right ulnar nerve became more marked, and absolute numbness developed over the anterolateral portion of the right leg, with marked hyperesthesia on the plantar surface of the foot. Wasting of the muscles of all extremities became so marked that the patient was "bedridden," and his right hand became so paralyzed as to be quite useless.

While all the aneurysms increased in size, that in the left femoral region grew most rapidly, until in the early part of February 1935 it had reached the size of a child's head. The skin over it became discolored and necrotic, and blood began to ooze from it. The patient was readmitted to the hospital on February 20.

At this time the findings were essentially as outlined, all the aneurysms having increased in size. The radial pulses were of normal volume, but the pulsations in both dorsalis pedis arteries, although present, were diminished as compared to their size on the patient's previous admission. The blood pressure in the right arm was 110 systolic and 94 diastolic; that in the left arm was 122 systolic and 92 diastolic.

Operations.—On February 25, with the patient under general anesthesia, a left rectus incision was made, and the left common iliac artery was exposed and ligated by means of linen tape. After operation the left leg was closely watched; at no time, however, did its color change. The skin temperature remained within normal limits, and there was no evidence of a deficiency in the circulation. The blood pressure in the left arm at this time was 130 systolic and 100 diastolic. Ten days later it had fallen somewhat, being 95 systolic and 80 diastolic in the right arm and 110 systolic and 85 diastolic in the left arm. The left leg was placed in the Pavaex

machine early in the postoperative period. The abdominal wound healed well, and there continued to be no change in the left leg. The aneurysm ceased to pulsate immediately after ligation of the artery and showed no signs of activity subsequently. It decreased somewhat in size, but three consecutive aspirations were performed through healthy tissue in an unsuccessful attempt to prevent necrosis of the skin over its anterior aspect. The patient's course continued favorably, but because the aspirations continued to yield fresh blood, on April 3, with procaine hydrochloride for local anesthetization a longitudinal incision was made on the medial aspect of the left thigh, the femoral artery was located and ligated, and a piece about 2 cm. in length was excised. The skin over the peak of the aneurysm sloughed, however, and despite proximal and distal ligation of the artery, blood continued to ooze from the sloughed area. Therefore, on April 6, with the patient under general anesthesia, a longitudinal incision was made over the aneurysm, the entire sac was evacuated of its clots, the femoral artery was doubly ligated within the sac and the cavity was packed. The packs were removed on the fourth postoperative day, and the wound

Fig. 1.—Aneurysm in the left femoral region just before ligation of the left common iliac artery, showing necrosis of the skin over the aneurysm.

was treated with saline solution. Under this treatment it gradually healed with clean and healthy granulations.

During this period the patient's greatest discomfort arose from the aneurysm in the right subclavian region, which was increasing in size. He was losing the function of his arm, and examination on June 15 revealed marked atrophy of the entire right arm, most noticeable in the right hand where the interosseus muscles were almost completely atrophied. He had an early clawhand, and neurologic examination revealed almost complete palsy of the median and ulnar nerves. While this was developing he had a great deal of pain in the arm and hand, which gave way to numbness, especially in the hand. On June 14, with the patient under general anesthesia, an incision was made over the medial portion of the clavicle on the right side, and the right innominate artery was tied off with linen tape, just proximal to its bifurcation into the carotid and subclavian arteries. Subsequent to this procedure the anuerysm ceased to pulsate, and no definite pulsation could be made out in either the radial or the temporal arteries. The blood pressure in the left arm after this procedure was 120 systolic and 80 diastolic.

It was remarkable to see the return of function and of feeling in the right hand and arm. At this time the patient could approximate the thumb and little finger, could extend and abduct the fingers moderately and could distinguish between blunt and sharp objects.

Course.—June 18: Complete physical examination on this date revealed the patient's general condition to be slightly altered from that at the time of admission. There was no demonstrable change in the heart, either as to size or sounds. The lungs were clear. The wound in the left femoral region was healed except for an area of about 4 cm. in length, 2 cm. in width and 3 cm. in depth, which was covered with clean granulations. The aneurysm in the left axilla did not seem to be causing any increase in symptoms and had not changed appreciably in size. The aneurysm in the right subclavian region yielded no pulsation. The operative wound was clean and healing well. The aneurysm in the right femoral region was not causing any symptoms but showed a slight increase in size. The aneurysm in the right popliteal space, which was by far the largest of all, did not appear to be causing any further symptoms, but it too was thought to be slightly increased in size.

The oscillometric readings (in units) were as follows:

Left Arm—B. P. 124/80		Right Arm—B. P. not obtained	
Upper part of arm	5.5	Upper part of arm	0.5
Forearm	4.0	Forearm	0.3
Left Leg		Right Leg	
Thigh	0	Thigh	5.0
Calf	0	Calf	3.5
Ankle	0	Ankle	3.5

The skin temperatures (C.) recorded at this time follow:

	Right	Left
Forehead	31.5	31.0
Cheek	30.5	30.5
Neck	34.0	33.0
Shoulder	32.0	33.0
Arm	32.0	31.0
Forearm	33.0	33.0
Dorsum of hand	34.0	34.0
Palm of hand	34.0	34.0
Chest	33.0	33.0
Abdomen	33.0	33.0
Thigh	33.0	32.5
Calf	32.0	30.5
Dorsum of foot	32.0	29.0
Plantar surface of foot	32.0	29.0

June 28: During the preceding week the patient's course was smooth and without complications. Examination on June 28 revealed the remainder of the aneurysms as previously stated, without change. The one in the right subclavian region still revealed no pulsation and had diminished in size. The wound had healed well, and the stitches had been removed. There was no radial pulsation felt in the right arm, and no temporal pulse could be palpated on the right side. The patient's greatest difficulty had been in the left knee, which still remained in a flexed position and was tender. Physical therapy afforded some relief.

The following oscillometric readings (in units) were obtained at this time:

	Right—B. P. 0/0	Left—B. P. 104/78
Upper part of arm	0.8	6.0
Forearm	0.5	6.0
Thigh	5.0	0.5
Calf	3.5	0
Ankle	3.5	0

July 5: During the preceding week there was one new development. Some pus discharged from the incision in the right clavicular region where the innominate artery was tied off. The wound was opened in one area, and a considerable quantity of pus was evacuated. The patient's general condition remained good. There were no pulsations felt in the right wrist or in the temporal region. The contracture of the left knee was responding favorably to physical therapy, the pain being less and the motion increased.

The following oscillometric readings (in units) were obtained:

	Right—B. P. 0/0	Left—B. P. 104/78
Upper part of arm	0.8	6.0
Forearm	0.5	6.0
Thigh	5.0	0.5
Calf	3.5	0
Ankle	3.5	0

July 12: During the preceding week there was little change in the patient's condition. Neither the right radial nor the temporal pulse could be felt. The aneurysm in the right subclavian region remained dead. The wound in the right clavicular region, which had been discharging pus, owing to through and through irrigations with saline solution had granulated and was not discharging any longer. The wound in the left femoral region was almost entirely healed. The patient had been sitting up on the edge of the bed with no ill effects. When he sat up it was seen that there was a slight purplish discoloration in the left leg and the right arm.

July 19: The wound in the right clavicular region, previously alluded to, was completely healed. There was no obvious change in any of the aneurysms. The one in the right subclavian region remained dead, with no evidence of either temporal or radial pulsation on the right side. The patient had been sitting on the edge of the bed. Motion in the left knee was gradually returning, and the contracture was reduced about 60 per cent.

July 26: During the preceding week there was little change in the patient's condition. The aneurysms remained as previously stated. The wound in the left groin and the wound in the right clavicular region were practically healed. Pulsations in the right wrist and temporal region were not felt. The patient sat at the edge of the bed every day, and while he was in the upright position cyanosis of the left leg and of the right arm was visible. General physical examination revealed nothing new.

The following oscillometric readings (in units) were obtained:

	Right—B. P. 0/0	Left—B. P. 118/82
Upper part of arm	0.5	4.5
Forearm	0.5	4.0
Thigh	3.5	0
Calf	2.5	0
Ankle	2.5	0

August 28: In the interval since July 26 the aneurysms remained essentially the same. The wound in the left inguinal region was well healed. During the first two weeks the patient's condition was good. On August 15 he had a temperature of 39 C. (102.2 F.), which persisted for three days. The area around the wound in the chest, which by this time was well healed, became indurated. A clamp was inserted, and some changed blood was evacuated. The fever persisted for three days and then subsided after adequate drainage was established. The wound cavity was irrigated thoroughly with saline solution. On August 18 a massive hemorrhage from this wound occurred, and the patient lost at least a liter of blood. The hemorrhage was well controlled by packs, and the patient's condition improved and at this time was very good. No pulsations were felt in the right wrist or in the temporal region. There was definite cyanosis of the left leg and right arm when the patient sat up.

The following oscillometric readings (in units) were obtained:

	Right—B. P. 0/0	Left—B. P. 120/80
Upper part of arm	0.1	5
Forearm	0.1	4
Thigh	3.5	0
Calf	2.5	0
Ankle	2.5	0

September 16: Since August 28 there had been little change in the patient's general condition. His blood count returned to normal, and he stated that he was quite comfortable. There was a definite progression of the aneurysm in the right popliteal region, which had increased both in length and in diameter. It measured 20 cm. in length, and the thigh at the center of this aneurysm measured 50.5 cm., as compared to 39 cm. for the left thigh at a similar position. The aneurysm in the left subclavian region had also grown considerably. The patient began to notice increased numbness in the left index finger and the same condition, but to a less extent, in the left middle finger. The wound in the left inguinal region was now well healed. There was only a slight degree of drainage. The wound in the right subclavian region had healed remarkably well. There was no purulent drainage at this time. General physical examination revealed nothing new. No pulsations were felt in the right wrist or in the temporal region. When the patient sat up in bed, cyanosis of the left leg and arm was visible. He felt that he was gaining some use of his left leg.

Neurologic examination revealed nothing new except for slight diminution of sensation over the left index finger and, to a lesser degree, over the left middle finger.

The following oscillometric readings (in units) were obtained:

	Right—B. P. 0/0	Left—B. P. 120/80
Upper part of arm	0	2.5
Forearm	0	2.0
Thigh	10.0	(over aneurysm) Trace
Calf	3.0	0.2
Ankle	1.5	0.2

The skin temperatures (C.) at this time were:

	Right	Left
Forehead	33.5	33.5
Cheek	32.5	33.0
Neck	33.5	34.5
Shoulder	33.5	33.5
Arm	33.0	33.5
Forearm	32.5	32.5
Dorsum of hand	31.5	32.5
Palm of hand	31.5	32.5
Chest	32.5	33.5
Abdomen	31.5	31.5
Thigh	30.9	31.5
Calf	30.0	30.5
Dorsum of foot	28.5	29.0
Plantar surface of foot	28.0	28.5

September 18: A right rectus incision was made, and the right common iliac artery was ligated with a catgut ribbon ½ inch (1.3 cm.) in width. Immediately after the ligation all pulsations ceased in the aneurysms in the inguinal and popliteal regions, and the extremity became cooler. There was no venous distention. The pulses of the popliteal, the posterior tibial and the dorsalis pedis arteries could not be felt. One hour after the patient was returned to the ward, oscillometric readings showed that there were no pulsations in the right leg as measured over the thigh, calf and ankle. The oscillometric reading preoperatively over the aneurysm was 10 units; postoperatively, it was 0 units. The extremity regained heat rapidly, so that one hour after operation the skin temperatures (C.) were as follows:

	Right	Left
Dorsum of foot	30	30.0
Plantar surface of foot	30	29.5
Calf	31	32.0
Thigh	32	33.0

Five hours after operation the oscillometric readings were 0, the extremities were warm, and no pulses could be felt in either foot.

September 19: Up to this time the patient's course had been uneventful. The right leg was warm; there were no pulsations in either aneurysm. The pulses of the popliteal, posterior tibial and dorsalis pedis arteries were still absent. Oscillometric readings were 0 over the thigh, calf and ankle.

The skin temperatures (C.) were as follows:

	Right	Left
Dorsum of foot	30.5	30.5
Plantar surface	29.5	30.5
Thigh	31.5	32.5
Calf	31.5	31.5

September 24: Since September 19 the patient's course had been satisfactory. The wound healed per primam, and all the skin sutures were removed on the sixth postoperative day. The aneurysm in the popliteal space had no pulsation. There was slight pulsation in the aneurysm in the right femoral region. The pulses of the popliteal, posterior tibial and dorsalis pedis arteries were still absent. Oscillometric readings (in units) over the calf, thigh and ankle were still 0.

Dorsum of foot	29.8	29.5
Plantar surface	29.0	29.5
Calf	31.0	31.0
Thigh	32.0	32.0

The skin temperatures (C.) were as follows:

	Right	Left

There was still slight drainage from the left groin. The wound cavity in the right subclavian region was now clean, and there was no drainage. The aneurysm in the left subclavian region had not changed noticeably since the last observation, and the patient's neurologic condition was unchanged.

October 8: The patient's course had been uneventful since the last report. The lower right rectus wound was healing. There was a small pus pocket at the side of the lower two through and through silver sutures. This was opened adequately and was irrigated with saline solution. The silver wires were still in place. There was definite, but slight, pulsation in the aneurysm in the right femoral region, which had also decreased in size. The preoperative measurement of the right thigh in the center of this aneurysm had been 50.5 cm., but now was 41.5 cm. The pulses of the popliteal, posterior tibial and dorsalis pedis arteries were absent bilaterally. The wound in the left groin was still draining slightly. The wound in the right subclavian region was fairly well healed. There were no pulsations of the aneurysm in the right subclavian region, and its size was essentially the same. The aneurysm in the left subclavian region had increased slightly in size. General neurologic examination revealed the persistence of the paralysis of the right ulnar nerve, both motor and sensory components being involved, as before. There was persistence of the absence of sensation over the anterior surface of the lower part of the left leg and dorsum of the foot, with hyperesthesia over the plantar surface of the left foot. Sensation of the right leg and foot was intact. There was an area of hypesthesia over the flexor surface of the left index finger, and the same condition persisted to a lesser extent over the distal portion of the flexor surface of the left thumb and the second finger.

The following oscillometric readings (in units) were obtained:

	Right	Left
Upper part of arm	Trace	4.2
Forearm	Trace	3.5
Thigh	0	0
Calf	0	0
Ankle	0	0
B. P., arm	0/0	120/80
B. P., calf	0/0	0/0

The readings for the skin temperature were essentially the same as those obtained on September 16, before ligation of the right common iliac artery.

October 16: Since October 8 the patient's course had been satisfactory. The lower right rectus wound was healing well. The infection at the site of the stay sutures, which were removed on the twenty-first postoperative day, had now practically subsided. There was definite pulsation in the aneurysm in the right femoral region, which had greatly decreased in size. The aneurysm in the popliteal space showed no pulsation, and there had been no change in its diameter in the

past few weeks. The pulses of the popliteal, posterior tibial and dorsalis pedis arteries were still absent bilaterally. There was still slight drainage from the wound in the left groin and in the right subclavian region. The aneurysm in the right subclavian region was free of pulsation and had definitely decreased in size. The one in the left subclavian region had increased in size. Atrophy was present in the muscles innervated by the left median nerve. Loss of sensation of the flexor surfaces of the left thumb, index and middle fingers had increased, and the palsy of the right ulnar nerve persisted.

The oscillometric readings (in units) were as follows:

	Right—B. P. 0/0	Left—B. P. 96/64
Upper part of arm	0	0.5
Forearm	0	1.0
Thigh	0	0
Calf	0	0
Ankle	0	0

The oscillometric readings and neurologic examination showed definitely increasing involvement of both the vascular and the nerve elements of the left arm. During the past eight days there was marked decrease in the oscillometric readings obtained on the left arm.

November 18: Since October 16 the patient's course had progressed satisfactorily. The lower right rectus wound had a persistent draining sinus. On November 17 a black silk suture was removed, and it was felt that healing should take place. The wounds in the left groin and right subclavian region had completely healed by this time, and the aneurysm in the right subclavian region was definitely smaller and showed no pulsation. The aneurysm in the left axilla had increased considerably in size, and the pulsation had increased. The patient had considerable pain in the left shoulder and in the left arm. The size and pulsation of the aneurysm in the right femoral region remained constant. The aneurysm in the popliteal space showed no pulsation, and the leg here measured 41.5 cm. in circumference. General physical examination showed no abnormalities in the heart and lungs.

Neurologic examination revealed an area of hyperesthesia over the left index finger on its flexor surface. The left hand could not be fully closed, and there was atrophy of the muscles supplied by the median nerve. Subjective numbness was present in the left index finger. Sensation in the right hand was improved. The atrophy in the muscles supplied by the ulnar nerve persisted, but the hypesthesia of the fourth and fifth fingers was less marked. The reflexes of the left arm were physiologic; those of the right were absent. Examination of the left leg revealed marked improvement, but the hyperesthesia of the plantar surface of the left foot persisted. The patient at this time could discriminate heat, pinprick, touch, etc., on the ventral surface of the lower part of the left leg and the dorsum of the foot, and the leg could be almost completely straightened. Sensation in the right leg was normal, as were reflexes in the lower extremities.

The following oscillometric readings (in units) were obtained:

	Right—B. P. 0/0	Left—124/80
Upper part of arm	0	1.5
Forearm	0	1.5
Thigh	0	0
Calf	0	0
Ankle	0	0

The skin temperatures (C.) were as follows:

	Right	Left
Upper part of arm	31.0	31.0
Forearm	32.0	31.0
Palm of hand	32.0	32.5
Thigh	32.5	32.0
Calf	32.5	31.5
Ankle	32.5	32.0
Dorsum of foot	33.0	32.0
Plantar surface of foot	32.5	31.5

December 10: The patient's general condition remained excellent. The infection at the site of the right rectus wound subsided, and the wound was completely healed.

With the patient under ethylene anesthesia, ligation of the left subclavian artery was performed. An incision 6 cm. long and parallel to and above the level of the clavicle was made, and the skin and platysma were divided. By means of careful dissection, the clavicle was isolated, and a section of it was removed. The distal fragment was then immobilized inferiorly. The subclavian artery was readily identified, as was the aneurysm. Blunt and sharp dissection were employed, the subclavian artery was ligated with a broad tape and the wound was closed. Throughout and after the procedure the patient's condition remained satisfactory. Directly after the operation the left extremity felt warm. The radial pulse was no longer palpable.

The oscillometric readings on the left arm were all 0.

The skin temperatures (C.) were as follows:

	Right	Left
Directly after operation:		
Forearm		30.0
Palm of hand		31.0
Dorsal surface of hand		31.0
Four hours after operation:		
Forearm		30.0
Hand		32.0
Eight hours after operation:		
Forearm	30.0	31.5
Hand	30.5	31.0
Twenty-four hours after operation:		
Forearm	30.5	31.5
Hand	31.5	32.5

December 26: The patient's postoperative course was uneventful, and the wound healed per primam. The aneurysm in the left subclavian region ceased to pulsate, and its size decreased rapidly. There was no objective change in the circulation of the hand and arm. All other wounds were now well healed. The aneurysm in the right popliteal space was unchanged. It was completely free from pulsation and constant in size. However, the aneurysm in the right femoral region had increased markedly in size and pulsated vigorously. A pulsating mass also appeared above Poupart's ligament, and the patient complained of pain in the region of the bladder and urgency in urination. He also experienced frequent attacks of shooting pain in the right lower abdominal quadrant and the right groin.

General examination revealed that there were no peripheral pulses. Neurologic examination was unchanged. The right ulnar palsy persisted, and there was an early median palsy of the left hand.

Oscillometric readings on all extremities were 0. The skin temperature remained unchanged since the last examination.

Jan. 1, 1936: The aneurysm in the right lower abdominal quadrant increased rapidly in size and formed an extremely large mass, filling almost the entire quadrant. On December 29 it doubled in size, and at 7 a. m., January 1, it ruptured into the abdominal cavity, causing the patient's death.

Autopsy.—Autopsy was performed four hours after death. The body was that of a well developed, well nourished white man 52 years of age and weighing 75 Kg. There was a marked pallor of the skin and mucous membrane. There were healed surgical incisions in both infraclavicular regions. On the right there had been a resection of the first rib. There were three surgical incisions in the lower abdominal region, all of which were well healed. In addition there was a well healed incision in the left femoral region. There were large firm masses in the left and right infraclavicular, right inguinal, right femoral and right popliteal regions. The extremities showed advanced muscular atrophy.

When the peritoneal cavity was opened, 100 cc. of thin bloody fluid was found. There was a large firm mass just above Poupart's ligament on the right. The wall of this mass was made up of thin friable tissue containing a large clot of fresh blood. There was a similar large clot in the region of the splenic flexure of the colon.

The organs, other than the circulatory system, showed no gross pathologic change. Therefore, only the heart and arterial system will be described in detail.

The heart weighed 320 Gm. It showed no gross pathologic change other than that the coronary arteries were thin walled and dilated. The dilatation took place within a few millimeters of their origin. These arteries showed only a slight degree of sclerosis of the intima.

The aorta was not dilated. Its wall was of the usual thickness, and arteriosclerosis of the intima as characterized by plaque formation was present only to a slight degree at the root of the aorta and in the region of its bifurcation. The innominate artery was not dilated. It was ligated with white linen tape just proximal to the origin of the right common carotid artery. Beneath the ligature the lumen was completely occluded, and the wall of the vessel was replaced by fibrous connective tissue. The right subclavian artery beyond the ligature was thin walled but not dilated. Three centimeters from its origin there was a large fusiform dilatation of the vessel, which on section was found to be made up of greatly thinned arterial wall containing a firm, laminated blood clot. The aneurysm was really made up of two continuous sacs, measuring 6.5 and 2 cm. in diameter, respectively. Firmly adherent to the posterior wall of the aneurysm and compressed by it were the major cords of the right brachial plexus. The axillary artery beyond the aneurysm was thin walled but not dilated.

The right and left common carotid arteries showed no gross pathologic change. The left subclavian artery showed a slight degree of arteriosclerosis. Seven centimeters from the aortic arch the vessel was ligated with white linen tape. The lumen of the vessel was just occluded by the ligature, beyond which there was a fusiform dilatation of the artery, measuring 5 by 4 cm. in diameter. On section, the aneurysm was found to be made up of a greatly thinned arterial wall containing a firm, laminated blood clot. The major cords of the left brachial plexus and the great nerves to the arm were compressed by the aneurysm.

As the celiac axis and the right renal and the left renal arteries left the aorta they became extremely thin walled and dilated. They measured 1.5, 1 and 1 cm. in diameter, respectively. These vessels showed a more advanced arteriosclerotic change than the vessels just described. However, the greatest pathologic change was in the media, which appeared irregularly thin and was waxy gray. The splenic artery showed a mild degree of arteriosclerosis and tortuosity. It showed a medial change similar to that described. The left common and left external iliac arteries showed advanced arteriosclerotic change. The left external iliac artery had been ligated with white linen tape just proximal to its origin. The lumen of the vessel

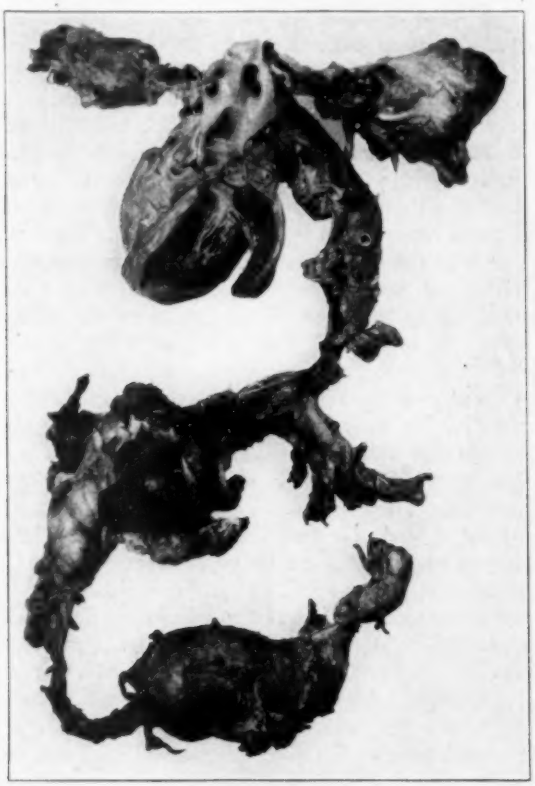

Fig. 2.—Photograph of autopsy material showing the major arteries and the position and size of the aneurysm.

was occluded both distal and proximal to the ligature by a firm laminated clot, which showed some early organization.

There was a moderate degree of arteriosclerosis of the right external iliac artery. The vessel contained a fusiform dilatation, beginning 3 cm. from its origin. This aneurysm was 15 cm. in length and varied from 10 to 5 cm. in diameter. It extended beneath Poupart's ligament and was compressed by it. The largest portion of the aneurysm was directed anteriorly. Here the wall was made up partially of thinned vessel and partially of peritoneum and fibrous connective tissue. There was a small portion of the aneurysm directed posteriorly the wall of which was made up partially of the wall of the vessel and partially of fascia covering the

iliolumbar muscle. The aneurysm had ruptured posteriorly along the sheath of the iliolumbar muscle. On section, the lower part of the aneurysm was found filled with a firm, laminated blood clot. The upper portion contained a moderately fresh blood clot. The linen ligature used in an attempt to occlude the aneurysm was present surrounding the aneurysm at the point of rupture. The right femoral artery was thin walled and showed advanced dilatation. There were many transverse bars of calcium in the media typical of the Moenckeberg type of arteriosclerosis. There were two large fusiform aneurysms in the popliteal space. The largest of these was 14 cm. in length and 7 cm. in its greatest diameter. The

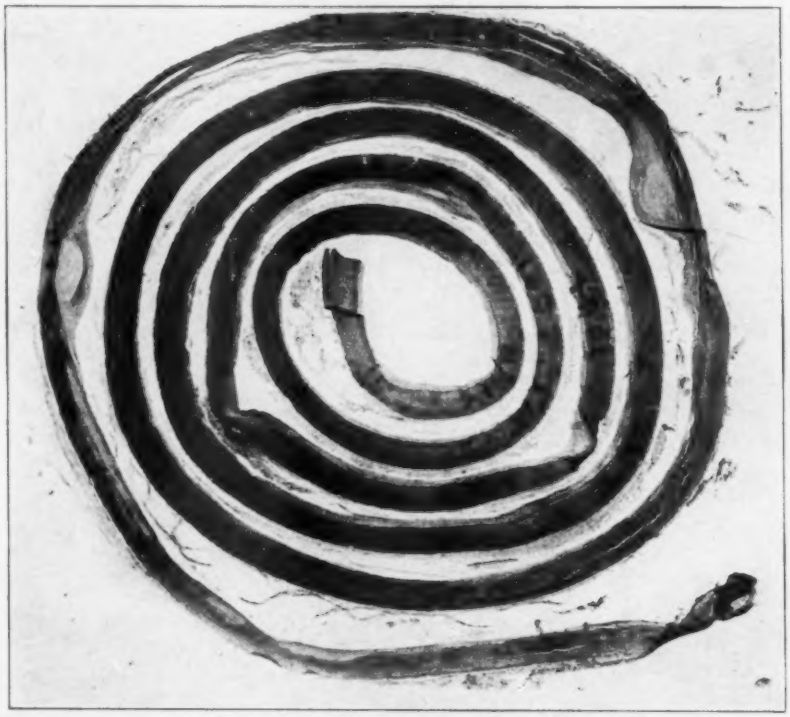

Fig. 3.—Section of the descending aorta, showing the method of cutting so that the entire aorta can be seen in one section. Two advanced lesions are to be seen. Weigert's elastic tissue stain; × 8.

smallest was 7 cm. in length and 2.5 cm. in its greatest diameter. They both were made up of an extremely thin vessel wall and contained a laminated blood clot.

The majority of the vessels were examined microscopically throughout their length by cutting rolled sections, as shown in figure 3. The sections were all stained with hematoxylin and eosin and with Weigert's elastic tissue stain. Special sections were stained for fat with sudan III. Masson's stain was used to differentiate muscle and connective tissue. The chromotropic substance was specially demonstrated by the use of thionine and polychrome methylene blue. Calcium was stained by the use of the von Kossa silver nitrate method. Brown's bacterial stain

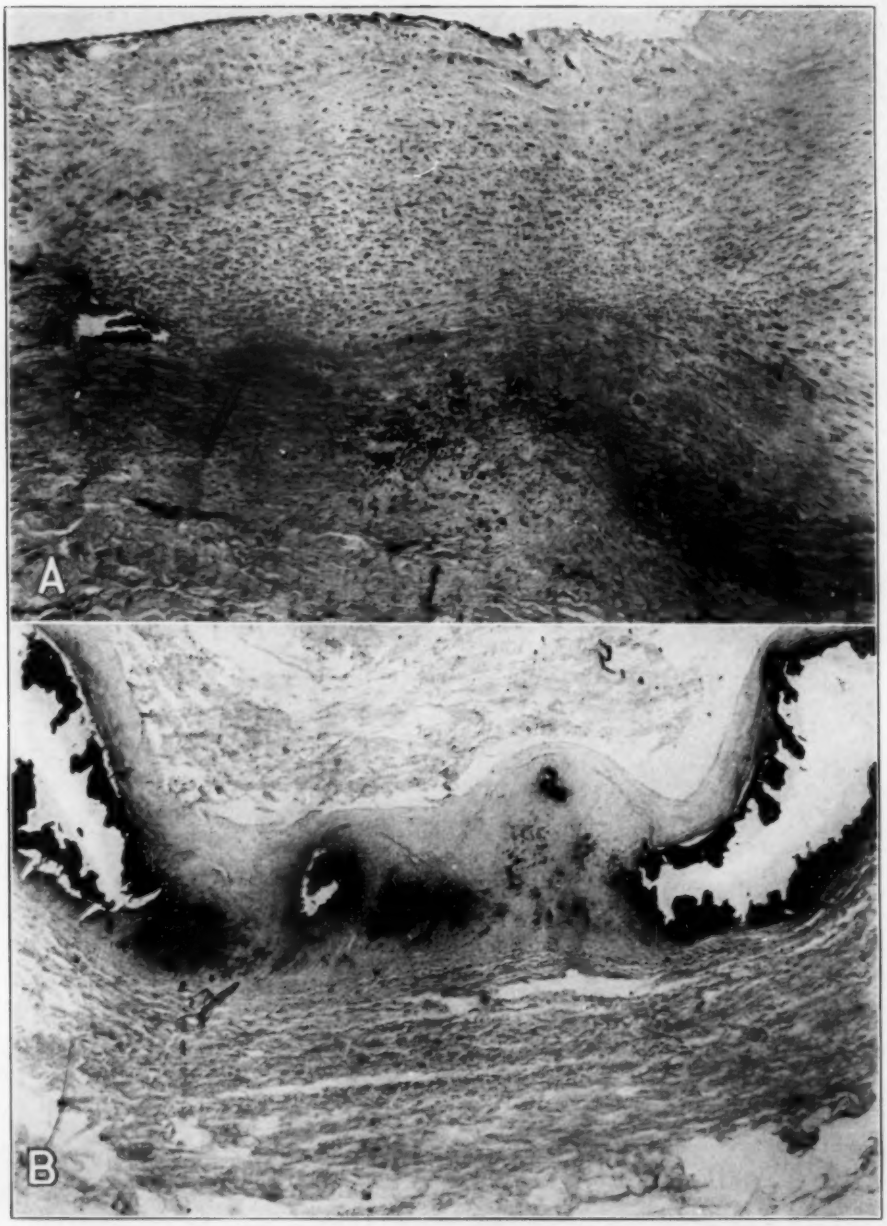

Fig. 4.—*A*, a section of the superior mesenteric artery, showing the greatly thickened intima and the underlying degeneration of the media. The section shows an area of early repair with an infiltration of the fibroblasts and new capillaries. Hematoxylin and eosin stain; × 69. *B*, a section of the right femoral artery. Typical large plaques of calcium are seen in the media. Between these in the muscle bundles and fibrous connective tissue are seen fine granules of calcium. Von Kossa stain; × 41.

and the Warthin-Starey stain for spirochetes were used on a few sections in an unsuccessful attempt to demonstrate micro-organisms.

Microscopically, there was a profound pathologic change present thoughout the media of all the arteries examined. The arterioles showed no pathologic change. The intima was not especially involved in this process. Arteriosclerosis, as represented by deposits of cholesterol and calcification of the intima, was present only to a slight degree. However, the intima was irregularly thickened throughout and had a peculiar undulating character.

The pathologic change taking place in the media was fundamentally one of degeneration. This was present to a profound degree in the muscular vessels. It was characterized by a degenerative change in the muscular fibers, with the result that these fibers appeared to be reduced in number and to be separated from each other by a granular basophilic substance. This substance stained red with thionine and polychrome methylene blue. It contained small droplets of fat when stained with sudan III. It had a finely granular deposit of calcium throughout and hypertrophy of the few remaining muscle fibers, shown in the sections by their increased size. In the muscular arteries the degenerative change had proceeded to a point where there was nearly complete absence of the media in some areas. In these vessels and also in the elastic arteries the elastic fibers were swollen and irregularly fragmented.

Throughout all the vessels there were areas of attempted repair by the formation of fibrous tissue. In the aorta where the degenerative change was the least severe the reparative process was much more satisfactory. As shown in figure 3, there were triangular areas of scar formation with the base toward the intima and extending nearly through to the adventitia. In the smaller arteries areas of repair were frequent (fig. 4*A*). Here there was an invasion of fibroblasts, collagen fibrils and newly formed capillaries into a degenerated portion of the media.

In the arteries of the lower extremities calcareous degeneration of the media was particularly prominent. In accordance with the suggestion of Klotz,[7] the Moenckeberg type of medial sclerosis, so well shown here, and the granular deposits of calcium in the media of the aorta were essentially manifestations of the same process, the calcium granules merely showing different degrees of coalescence. We have endeavored to show this in figure 4*B*. The von Kossa stain here showed not only large plaques of calcification in the media but beginning fine granular calcification in the degenerating muscle bundles and fibrous connective tissue between the plaques.

In the walls of the aneurysms themselves the same degenerative changes were present as were found in the media. In the section in figure 5*A*, which was taken from the wall of the aneurysm in the right subclavian region, a profound degenerative change of both the muscularis and the elastica was evident. The swelling and fragmentation of the elastic fibers could be especially well seen.

In areas in which the lumen of the vessel had been occluded by a ligature the wall of the vessel was replaced by loose connective tissue, which showed an infiltration of lymphocytes and plasma cells with an occasional foreign body giant cell. Such an area is shown in figure 5*B*.

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7. Klotz, O.: Studies upon Calcareous Degeneration, J. Exper. Med. **8**:322, 1906.

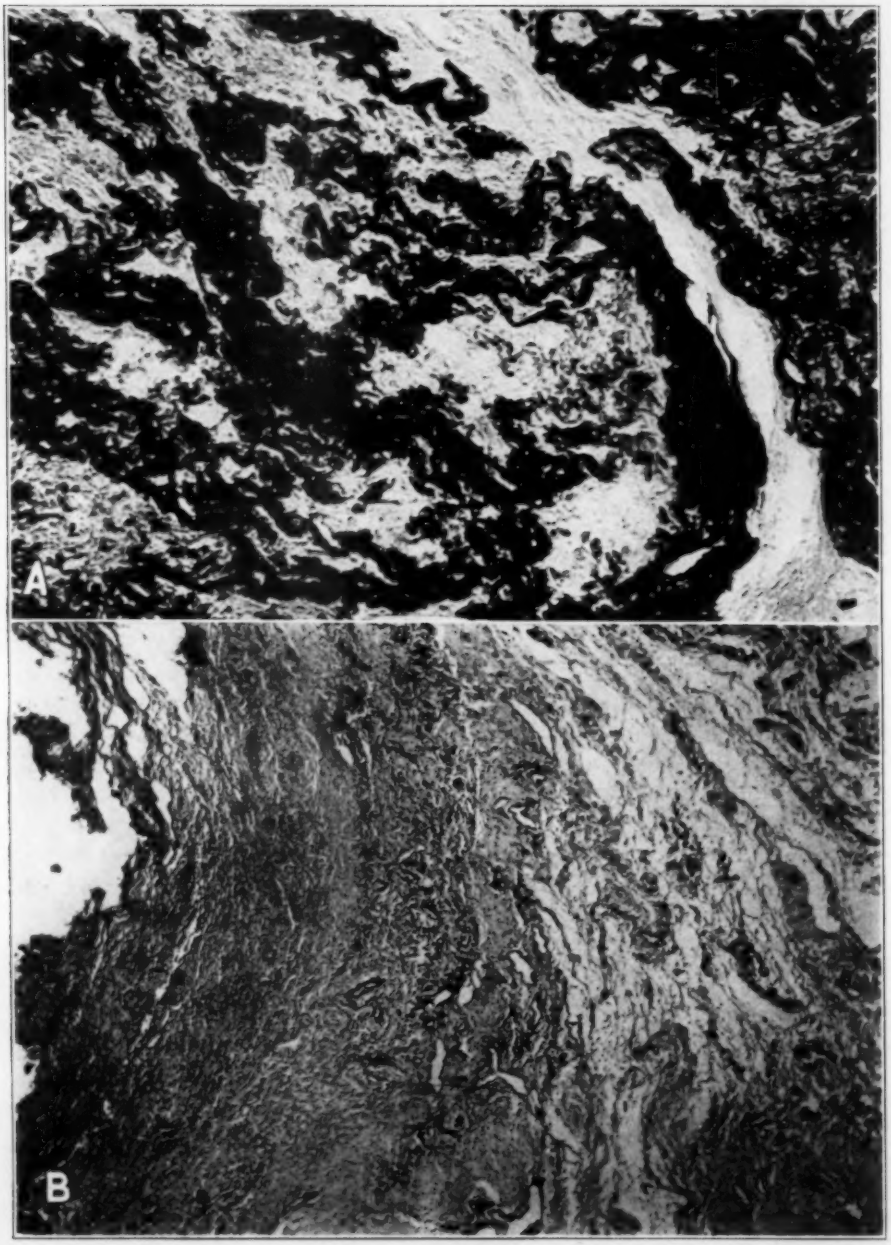

Fig. 5.—*A*, a section of the wall of the right subclavian aneurysm, showing swelling and fragmentation of the elastic fibers interspersed with degenerated muscle bundles; × 207. *B*, a section of the innominate artery beneath the ligature of linen tape; × 69. The wall is replaced by fibrous connective tissue which is infiltrated with lymphocytes and a few foreign body giant cells.

COMMENT

The majority of the cases of multiple aneurysms reported in the literature are either syphilitic or mycotic in origin and as such have no resemblance to the picture herein presented. The small multiple aneurysms associated with periarteritis nodosa have little resemblance to the lesion we have described. Also, the frequently reported cases of multiple aneurysms of the circle of Willis are morphologically and etiologically different.

Literature on diseases of the media is relatively scanty. Scarpa in 1804 has the distinction of being the first to state that no aneurysm could arise without some disease of the media. Francis Welch [8] was not only the first to describe syphilitic aortitis clearly but also the first to describe degenerative lesions of the aorta, unassociated with aneurysm and caused, as he stated, by rheumatism or alcohol. Johnson [9] recognized the existence of hypertrophy of the media, more particularly in the smaller arteries. Thoma [10] laid stress on weakening and degeneration of the media of the aorta and larger arteries as predisposing to sclerosis of the intima. It was Moenckeberg,[11] however, who made the first serious study of disease of the media as a separate entity. Weiszmann and Neumann [12] and Manchot [13] stressed the association of the formation of aneurysms with arteriosclerosis and fatty degeneration of the media, especially of the elastic fibers. Dmitrijeff [14] stated that the fatty degeneration of the elastic fiber is the earliest sign of lesions of this coat.

Klotz,[15] in a monograph on diseases of the media, classified the degenerative lesions of the media under the headings of atrophy, necrosis and fatty, calcareous, amyloid and hyaline degeneration. They are not

8. Welch, F. H.: Aortic Aneurysm in the Army, Med.-Chir. Tr. **11**:59, 1876.

9. Johnson, G.: On Certain Points in the Anatomy and Pathology of Bright's Disease of the Kidney, Med.-Chir. Tr. **51**:57, 1868.

10. Thoma, R.: Ueber die Abhängigkeit der Bindegewebsneubildung in der Arterienintima von den mechanischen Bedingungen des Blutumlaufes, Virchows Arch. f. path. Anat. **105**:1, 1886.

11. Moenckeberg, J. G.: Ueber die reine Mediaverkalkung der Extremitätarterien und ihr Verhalten zur Arteriosklerose, Virchows Arch. f. path. Anat. **121**:141, 1903.

12. Weiszmann, F., and Neumann, S.: Ueber Veränderungen der elastischen Fasern in den Gefässwänden infolge von Arteriosklerose, Allg. Wien. med. Ztg. **35**:291, 1890.

13. Manchot, C.: Ueber die Entstehung der wahren Aneurysmen, Virchows Arch. f. path. Anat. **121**:104, 1890.

14. Dmitrijeff, A.: Die Veränderung des elastischen Gewebes der Arterienwände bei Arteriosklerose, Beitr. z. path. Anat. u. z. allg. Path. **22**:207, 1892.

15. Klotz, O.: Arteriosclerosis: Diseases of the Media and Their Relation to Aneurysm, Lancaster, Pa., New Era Printing Co., 1911.

necessarily associated with disease of the intima. The change is widespread but occurs most severely in the muscular arteries. The degeneration occurs in the muscle fibers but at a later stage may involve the elastic fibers as well. It is in the areas formerly occupied by muscle that calcium and fat are deposited. Whether the calcium occurs in plaques, as described by Moenckeberg and found in this case in the femoral arteries, or is present in fine granules, as seen in the aorta in this case, is dependent, according to Klotz, on the density of the elastic fibers. Klotz stated that whatever the type of degeneration of the media may be, the weakening of this coat provides the physical criteria for the formation of an aneurysm. Although he mentioned no specific cases, he stated that sclerosis of the media is often associated with peripheral diffuse dilatation of the arteries or multiple sacular aneurysms, which are rarely noted at autopsy and do not attain clinical significance.

More recently the product of the muscular degeneration has been called chromotropic substance by Schultz.[16] Gsell[17] and Erdheim[18] described this type of degeneration in the aorta associated with cyst formation and leading to spontaneous rupture. Moritz[19] and Klotz and Simpson[20] reported similar cases. Cellina[21] reported a disseminated type of the disease occurring in old age.

The etiology of these degenerative changes is as obscure as that of arteriosclerosis in general. That certain bacterial infections can produce disease of the media is well recognized. Foremost among these is syphilis. In our own case this can be ruled out, both clinically and pathologically. The pyogenic bacteria are capable of producing lesions in the media with mycotic aneurysms. There was a history of "blood poisoning" in this case twenty-eight years before death. The lesion in the media, however, is not inflammatory. Wiesel and Löwy[22] pointed

16. Schultz, A.: Pathologie der Blutgefässe, Ergebn. d. allg. Path. u. path. Anat. **280**:65, 1931.

17. Gsell, O.: Wandnekrosen der Aorta als selbständige Erkrankung und ihre Beziehung zur Spontanruptur, Virchows Arch. f. path. Anat. **270**:1, 1928.

18. Erdheim, J.: Medionecrosis aortae idiopathica, Virchows Arch. f. path. Anat. **273**:454, 1929; Medionecrosis aortae idiopathica cystica, ibid. **276**:187, 1930.

19. Moritz, A. R.: Medionecrosis Aortae Idiopathica Cystica, Am. J. Path. **8**:717, 1932.

20. Klotz, O., and Simpson, W.: Spontaneous Rupture of the Aorta, Am. J. M. Sc. **184**:455, 1932.

21. Cellina, M.: Medionecrosis disseminata aortae, Virchows Arch. f. path. Anat. **280**:65, 1931.

22. Wiesel, J., and Löwy, R.: Studien zur Pathologie des Kreislaufs, Wien. Arch. f. inn. Med. **1**:197, 1920.

out that diphtheria, typhoid, scarlet fever, pneumonia and influenza may be associated with degeneration of the media, but in this case there is no history of these infections.

It has been shown by Klotz [23] and Adler and Hensel [24] that numerous drugs and poisons, for example, nicotine and epinephrine, will produce medial degeneration experimentally in animals. In fact, Klotz produced true multiple aneurysms in rabbits by the long continued injection of epinephrine. The bearing of these observations on the disease in man is not conclusive.

Thayer and Fabyan [25] pointed out that vessels subjected to unusual strain, as the femoral arteries of persons who remain on their feet all day, show similar degenerative changes. It is interesting to note that in this case the aneurysms occurred at a site where the artery passed over an articulation. This is certainly the point where maximum movement in the arterial wall might be expected and where the artery might be subjected to maximum strain.

That old age can produce quantitative and qualitative changes in the elastic tissue has been shown by Aschoff.[26] Our own patient was a relatively young person who showed scant evidence of the arterial changes associated with advanced age.

From the point of view of the surgical treatment of aneurysms, the case presents several matters of interest. First, it emphasizes that the most meticulous asepsis should be employed in all operations of a vascular nature lest infection ensue and give rise to secondary hemorrhage. In this case the first aneurysm attacked was already infected due to sloughing of the skin over it, and from this area moderately severe secondary hemorrhage occurred, for which it was necessary to remove the clot from the aneurysm and ligate the vessel again.

The second aneurysm attacked was that in the right subclavian region, for the cure of which the innominate artery was ligated, while the wound of the infected aneurysm in the left femoral region was still draining. This wound became infected also; it was treated with diluted solution of sodium hypochlorite, U. S. P., and healed, but subsequently the infection recurred and gave rise to severe secondary hemorrhage which, however, was satisfactorily controlled by packing.

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23. Klotz, O.: Experimental Production of Arteriosclerosis, Brit. M. J. **2**:1767, 1906; Experimentelle Arbeits-Arteriosklerose, Centralbl. f. allg. Path. u. path. Anat. **19**:535, 1908.

24. Adler, I., and Hensel, O.: Intravenous Injections of Nicotine and Their Effects upon the Aorta of Rabbits, J. M. Research **15**:229, 1906.

25. Thayer, W. S., and Fabyan, M.: Studies on Arteriosclerosis, with Special Reference to the Radial Artery, Am. J. M. Sc. **134**:811, 1907.

26. Aschoff, L.: Ueber Atherosklerose und andere Sklerosen des Gefässystems, Beihefte z. Med. Klin. **4**:1, 1908.

Another point of surgical interest is the effect of the ligatures on the walls of the vessel, as in this case all ligations were performed with linen tape ½ inch (1.3 cm.) in width and tied just tightly enough to obliterate the pulsation in the vessel distal to the ligature. At postmortem examination all ligatures were intact except that placed on the right common iliac artery, which had obviously cut through the wall of the artery, giving rise to the aneurysm, rupture of which was the immediate cause of death. Histologic study of the arteries at the site of ligation showed that the ligatures in all instances had caused necrosis of the underlying vessel wall with replacement by fibrous tissue.

From the standpoint of the physiology of the circulation in the periphery after ligation of the major vessel to an extremity, it is interesting to note that during the relatively long period which elapsed between the appearance of the aneurysms and the vascular ligations, a sufficient collateral circulation developed so that there was little change in skin temperature distal to the ligature and no signs of circulatory insufficiency so long as the patient remained prone. However, cyanosis promptly appeared when the venous pressure was raised by the patient assuming a sitting posture.

The long period between the successive ligation of the left iliac, innominate, right iliac and left subclavian arteries was probably responsible for the fact that no clinical evidence of cardiac change was demonstrable. The constant blood pressure is no doubt to be explained on the same basis. It should be noted in this regard, however, that the patient remained in bed at absolute rest for almost his entire stay in the hospital with the least possible load on his circulatory system.

The immediate cause of death was the rupture of an aneurysm of the left common iliac artery, brought about by the giving way of the wall at the site of ligation with a linen tape. Why this ligature should have cut through when the left iliac and innominate arteries, which had been ligated for a much longer time, remained intact is something of a mystery and yet stresses the danger inherent in ligation of large arteries. The wall of a large artery beneath a ligature always undergoes necrosis and replacement with fibrous tissue. If this replacement takes place rapidly enough and the pressure within the vessel is not too great, the ligation is successful; but here it is evident that such was not the case—the ligature cut through and gave rise to a fatal hemorrhage.

SUMMARY

A case of multiple aneurysm of the major peripheral arterial trunks is reported. The basic pathologic change responsible for the aneurysm was a degeneration of the tunica media characterized by loss of muscle

fibers, swelling and fragmentation of elastic fibers, disseminated foci of calcification and fibrous replacement of the media. Some fibrous thickening of the intima was also present. The process, which differs from nodular intimal arteriosclerosis and shows no evidence of inflammation, is probably related to the medial arteriosclerosis of Moenckeberg.

In the treatment of the aneurysm, all the primary branches of the aorta leading to the head and extremities, except the left carotid artery, were successively ligated. Some studies on the effects of these ligations on the peripheral circulation are presented.

ANHYDREMIA AS A FACTOR IN DEATH FROM AUTOLYTIC PERITONITIS

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In 1924 Mason and Davidson published reports of experiments which directed attention to the toxic effect of fresh liver implanted in the peritoneal cavity. Later Ellis and Dragstedt [1] (1930) repeated this work and came to the conclusion that the death of the animals in which liver had been placed in the peritoneal cavity was due to the severe peritonitis caused by an organism similar to Bacillus Welchii. Peritonitis did not occur when pieces of adult or fetal liver which had been autoclaved were introduced into the abdomens of dogs. According to these authors the infection came from the liver in which the bacteria persisted in a latent state until stimulated to activity by the asphyxia of the liver tissue.

Andrews and Hrdina [2] repeated these experiments, as they did not believe that when animals died in so short a time (from twenty to twenty-four hours) death could be attributed to infection alone. In spite of the fact that they recovered an organism similar to B. Welchii from the implanted liver and fluid in the abdomen, they believed that the death of the animal was due to the toxic action of the autolyzed liver tissue. The changes which were noted after death were hemorrhage into the peritoneum and free fluid in the abdominal cavity (from 300 to 500 cc.). Death was thought to be caused by a severe infection from a gas-producing organism, which probably entered the abdominal cavity through an altered intestinal wall, for such an infection may follow also implantation of sterile material. The toxic agent derived from autolyzed liver is soluble in water, is thermostable, is precipitated by alcohol and chloroform, gives a biuret reaction and is dialyzable with difficulty. Therefore, it is probably to be classified among the albumoses.

From the Surgical Clinic of the Royal University of Naples, Prof. L. Torraca, Director.

1. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. **20**:8-16 (Jan.) 1930.

2. Andrews, E., and Hrdina, L.: The Cause of Death in Liver Autolysis, Surg., Gynec. & Obst. **52**:61-66, 1931. Andrews, E.; Rewbridge, A. G., and Hrdina, L.: Causation of Bacillus Welchii Infections in Dogs by Injection of Sterile Liver Extracts or Bile Salts, ibid. **53**:176-181, 1931.

Vallone [3] performed a series of experiments in which pieces of different organs and tissues (liver, spleen, pancreas, muscle and kidney) were placed in the abdominal cavity in the fresh state after being autoclaved. The most striking change which was noted in all the experiments was an intense hyperemia of the peritoneum, the presence of varying amounts of a serohemorrhagic fluid and a more or less definite fatty change in the liver and spleen. The cultures from the fluid in the abdominal cavity and implanted material (simple and Tarozzi's broth) were negative. In almost all the cases the implanted tissue was encapsulated by the great omentum. Vallone thought that homo-implants and hetero-implants into the abdominal cavity caused grave symptoms because of the absorption of protein materials following necrosis. These substances are not inactivated by heat, and death follows, even when the implants have been autoclaved. Applying his experimental results to the clinic, he expressed the belief that death in some cases of acute pancreatitis and in some cases of abdominal contusion in which the hemorrhage is not large enough to cause death can be explained on the basis of the absorption of products from contused organs, such as the liver, spleen and kidney. The clinical syndrome in some of these cases is not unlike that which can be produced experimentally.

Mason and Lemon [4] continued work along this line. The results of their experiments caused them to believe that three factors contributed to death from autolytic peritonitis. The first is a toxic substance formed in the liver during autolysis, since from 7 to 8 cc. of a saline extract given intravenously is enough to produce death of the experimental animal. The second factor, which Mason and Lemon mentioned and Ellis and Dragstedt overemphasized, is the Welch bacillus, for a pure culture of this organism injected into the peritoneal cavity does not produce changes comparable to those found after the autolysis of the liver. The third factor is anhydremia. Free fluid is always found in the peritoneal cavity of dogs which have died after implantation of liver into the peritoneum. The quantity of free fluid is equal to from one third to one half of the total volume of blood. With the escape of fluid into the peritoneal cavity, these authors noted considerable increase in the concentration of the blood, due to a reduction in the volume of blood plasma and blood serum and an increase in the percentage of fibrin.

Mason and Lemon stated that their experiments justified them in assuming that the liver tissue autolyzed in the peritoneal cavity liberated

3. Vallone, D.: La peritonite autolitica consecutiva a trapianto nell'addome di organi e di tessuti, Riforma med. **47**:1293-1297 (Aug. 24) 1931.

4. Mason, E. C., and Lemon, C. W.: Anhydraemia as a Possible Cause of Death in Liver Autolysis, Surg., Gynec. & Obst. **55**:427-431, 1932.

substances which cause a chemical peritonitis followed by an increased permeability of the abdominal viscera and that the use of drains shortened rather than lengthened the life of the animals.

In 1935 I [5] published the results of work which I had done on this subject. I experimented on rabbits, implanting into their abdominal cavities varying quantities of liver tissue recently removed under sterile conditions from animals of the same species. I demonstrated that the rabbit's liver does not contain the Welch bacillus or other pathogenic organisms to which have been attributed the cause of death of animals into which liver tissue has been implanted. I also demonstrated that not all the rabbits into which liver had been implanted died within a few hours and that the death of the animals was not in direct or close relation to the amount of liver implanted. The peritoneal fluid found in the animals which died a short while after implantation was sterile.

In my work cultures from the liver, spleen and bone marrow were always positive for the colon bacillus, even when cultures of the fluid in the peritoneal cavity were negative. The presence of these organisms in the liver, spleen and bone marrow—not normally found there—would indicate that they had probably passed through the intestinal wall at points adherent to the implanted liver, where there were gross and microscopic evidences of inflammation, and then entered the blood stream to be deposited in the liver, spleen and bone marrow. When these foci of inflammation were not present the animal did not die. The presence of colon bacilli cannot be regarded as a preagonal phase, because they were found before the beginning of this phase. Neither can their presence be regarded as due to contamination during operative manipulations, for if such were the case the peritoneal fluid would have been infected, but it was always sterile. Very small amounts of peritoneal exudate were found in the rabbits which died a short while after the implantation of homologous liver, while Andrews and Hrdina found from 300 to 500 cc. in their animals. Vallone and Mason and Lemon found relatively large quantities. According to Mason and Lemon the peritoneal fluid equals from one third to one half of the blood volume of the animal, and therefore anhydremia cannot be considered the cause of death. Having noticed that there were but a few drops of fluid in the peritoneal cavity of the rabbits which had died soon after the introduction of fresh liver, I undertook other experiments in which dogs were used in order to repeat the experiments of the American authors and to study the relation of anhydremia to death. The data on these experiments are given in the accompanying table.

5. Iesu, G.: Ricerche batteriologiche sulla peritonite autolitica, Gior. di batteriol. e immunol. **15**:109-120, 1935.

EXPERIMENTAL WORK

In these experiments the same operative technic was employed as on the rabbits. A median laparotomy was performed under aseptic precautions, and a piece of liver that had been removed from another dog and previously weighed and sterilized was dropped into the abdominal cavity. The abdominal incision was then closed. All the dogs with the exception of the sixth showed weakness after five or six hours, which increased with time up to death.

Examination of the blood (Wu method) showed an increase in the percentage of fibrin, which in experiment 4 increased from 3.5 before the operation to 7.25 sixteen hours after.

The autopsy performed on some animals in the preagonal state showed a serohemorrhagic fluid (from 310 to 600 cc.) in the peritoneal cavity and evidences of a hemorrhagic enteritis, diffuse peritonitis and fatty degeneration of the spleen and liver. The implanted piece of liver

Data on Experimental Work

Experiment No.	Wt., Kg.	Implanted Liver, Gm.	Percentage of Implanted Liver	Length of Time Before Death	Blood Volume	Quantity of Peritoneal Fluid, Cc.	Approximate Relation
1.....	15.5	80	0.50	25 hr.	1.192	400	1/3
2.....	21.5	110	0.50	19½ hr.	1.653	400	1/4
3.....	15.93	175	0.10	16 hr.	1.220	600	1/2
4.....	12.8	50	0.39	26 hr.	0.987	310	1/3
5.....	15.4	80	0.51	24 hr.	1.187	400	1/3
6*....	16.2	60	0.37	48 days	1.246	none	...

* The implanted piece of liver was encapsulated by the great omentum.

was reduced in size and of a brown color. Adhesions were found between the piece of liver and the mesentery of the small bowel, the anterior wall of which in one animal presented areas of necrosis. A piece of the liver which was implanted was placed in simple and Tarozzi's broth in all the experiments to determine whether or not it was free from germs. The cultures were constantly sterile. The results confirm the conclusions of Wolbach and Saiki, Vallone, Berg, Zau and Jobling and Trusler and Reeves [6] that liver of the living dog does not contain pathogenic organisms. On the other hand, the free fluid in the peritoneal cavity, of which I have made cultures (simple and Tarozzi's broth), has always contained numerous intestinal bacteria. I have never found, however, B. Welchii or similar bacteria.

6. Trusler, H. M., and Reeves, J. R.: The Significance of Anaerobic Organisms in Peritonitis Due to Liver Autolysis: Bacterial Flora of Liver and Muscle of Normal Dogs, Arch. Surg. **28**:479-491 (March) 1934. Trusler, H. M.; Reeves, J. R., and Martin, H. E.: Significance of Anaerobic Organisms in Peritonitis Due to Liver Autolysis: A Bacteriologic Study of the Peritoneal Exudates, ibid. **30**:371-393 (March) 1935.

COMMENT

My work confirms that of Andrews and Hrdina, Vallone and Mason and Lemon. Like these, I have found relatively large quantities of peritoneal fluid and a considerable increase in the concentration of blood, with lowering of the volume of blood plasma and blood serum and an increase in the percentage of fibrin.

Cultures from the implanted liver have never shown B. Welchii to which the death of the animal could be attributed. Some authors (Wolbach and Saiki, Trusler and Reeves and others) have found an anaerobic bacillus in cultures taken from the liver. This organism produces gas, is gram-positive, does not ferment sugar, does not produce endotoxins and when injected into the muscles of guinea-pigs is not pathogenic. It has been confused with pathogenic bacilli. Too frequently anaerobic, gas-producing organisms have been regarded as B. Welchii. These authors expressed the opinion that this mistake has been made frequently and that some workers, such as Ellis and Dragstedt, have as a result considered B. Welchii and similar organisms as the lethal factor.

Mason and Lemon injected a pure culture of B. Welchii into the peritoneal cavities of dogs, and their results were in no way comparable to those found in the autolytic peritonitis under discussion. The fact that the peritoneal reactions can be produced by implants of sterile liver speaks against the peritoneal change being bacterial in origin (Andrews and Hrdina, Vallone and Trusler and Reeves).

The results obtained in my experiments would seem to show that the theory of a bacteremia developing from the liver transplant is tenable neither for dogs nor for rabbits. However, they confirm the theory of a chemical peritonitis, which causes an increase in the permeability of the abdominal viscera and considerable free fluid in the peritoneal cavity. The bacteria in the fluid are of intestinal origin. They have been demonstrated by Mason and Lemon.

Anhydremia following the implantation of pieces of liver in the abdominal cavity cannot be regarded as a constant cause of death, for in my work I have shown first in rabbits and then in dogs that under identical conditions the rabbits died in the same length of time as the dogs, even when there was so little fluid in the peritoneal cavity as to preclude anhydremia as a factor in the cause of death.

DISCHARGES FROM THE NIPPLE

THEIR CLINICAL SIGNIFICANCE AND MAMMOGRAPHIC INTERPRETATION

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AND

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OMAHA

Nature frequently enshrouds pathologic changes of the mammary gland in a group of confusing symptoms. Correct interpretation of these inconstant and ever changing syndromes sorely taxes the diagnostic ingenuity of the physician. No two persons react similarly to identical lesions. A papilloma of the milk ducts may initiate a bloody discharge from the breast of one patient and a serous secretion from the breast of another, while there may be no discharge from the breast of a third patient. Likewise, a small infiltrating deep-seated carcinoma may be distinct and easily palpable in one breast and indefinite and indeterminable in another. Pain may or may not announce the presence of an intracystic hemorrhage, a growing neoplasm, a distended cyst or an infection of the milk ducts.

A discharge from the nipple of a nonlactating breast is frequently the initial symptom which impels the patient to seek medical advice. While the abnormal discharge is indicative of a pathologic change within the ductal and secretory systems, it affords but scant information concerning the provocative factor. It is evident that the amount, color, consistency and odor of the discharge depend not only on the nature of the causative lesion but on the degree to which the secretion is altered before reaching the surface of the nipple. If the bleeding neoplasm is situated near the orifice of the duct, the escaping fluid is frankly hemorrhagic, but if the tumor is deep within the matrix, the fluid assumes a serosanguineous or a serous character or even a brownish chocolate color due to the degeneration of the retained blood and its admixture with other secretions from the duct. The character of the discharge may also be altered by infection, necrosis or extension of the causative lesion. For example, a simple cyst may produce a clear serous secretion, but if a cyst is invaded by pathogenic organisms, the discharge assumes a purulent character.

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Unfortunately, conditions which produce these confusing discharges likewise fail to establish identifying physical signs. In spite of the accessibility of the mammary glands, small infiltrating carcinomas, papillomas, dilated lactiferous ducts and compressible cysts can seldom be palpated. An appreciation of these diagnostic difficulties caused Cutler [1] to introduce his transillumination studies. While some neoplasms can be visualized by this procedure, the vast majority possess the same translucency as the matrix of the breast, thus making differentiation extremely difficult. Soft tissue roentgenography, as popularized by Lockwood and Stewart,[2] has also failed to depict the identifying characteristics of mammary neoplasms clearly. The frequency with which exploratory biopsy is performed confirms the foregoing statements.

All pathologic conditions associated with a discharge from the breast must, of necessity, originate within or secondarily involve the ductal system. Any procedure, therefore, which actually visualizes the lactiferous ducts should possess considerable diagnostic value. During the past two years a method has been developed for visualizing the breast by means of contrast roentgenograms.[3] A radiopaque material, such as stabilized thorium dioxide, is introduced into the milk ducts by cannulating their orifices with a blunt no. 26 gage needle. Stereoscopic roentgenograms then give an accurate anatomic pattern of the ducts. Any abnormalities, such as alterations in the size, shape or conformation of these ducts, can be detected readily and the causative agent identified. An experience with more than three hundred and seventy-five contrast mammograms clearly demonstrates that they are invaluable in the diagnosis of lesions of the breast. Mammographic studies are particularly effective in visualizing pathologic states which are responsible for discharges from the nipple, and they also contribute valuable information concerning the evolution of such syndromes. Corroborative evidence can best be furnished by the presentation of actual cases.

BLOODY DISCHARGES

A frank hemorrhagic or serosanguineous discharge from the nipple indicates that the mammary gland is undergoing some pathologic change. While such a symptom constitutes a definite warning, unfortunately it is

1. Cutler, Max: Transillumination as an Aid in the Diagnosis of Breast Lesions, Surg., Gynec. & Obst. **47**:721, 1929.

2. Lockwood, I. H., and Stewart, W.: The Roentgen Ray Examination of the Breast, J. Missouri M. A. **29**:557, 1932.

3. Hicken, N. Frederick: Mammography: The Roentgenographic Diagnosis of Breast Tumors by Means of Contrast Media, Surg., Gynec. & Obst. **64**:593 (March) 1937. Hicken, N. Frederick; Best, R. Russell; Moon, C. F., and Harris, T. T.: The Preoperative Visualization of Breast Tumors, J. A. M. A. **108**:864 (March 13) 1937.

associated with such a variety of pathologic conditions that it possesses but little diagnostic value. Stowers [4] concluded that a bloody discharge occurring in the absence of trauma or a palpable tumor is most likely to be caused by a papilloma of the milk ducts. Adair [5] expressed the belief that it is indicative of a carcinoma of the milk ducts. Tapie [6] stated that such a loss of blood is due to a benign papillomatous growth or to an "endocaninular dendritic carcinoma." Greenough and Simmons [7] studied twenty cases of cystadenoma and found that in eleven there was a hemorrhagic seepage from the nipple; a malignant growth was discovered in three. Miller and Lewis [8] maintained that a bleeding nipple is not necessarily a sign of a malignant growth, for the discharge may originate in an adenocystic disease of the breast. Cheatle and Cutler [9] pointed out that such a discharge is usually associated with a papilloma, but that it affords no information as to whether the tumor is benign or malignant. Von Saar [10] firmly maintained that there is no relationship between a malignant lesion of the breast and a bleeding nipple. Paget's disease, tuberculosis, chronic cystic mastitis,[11] fibro-adenoma, trauma and vicarious menstruation [12] are other conditions associated with a hemorrhagic discharge from the milk ducts.

One is forced to admit that the symptom of a "bleeding nipple" has no diagnostic significance, yet it is imperative that the primary cause be accurately determined. Contrast mammographic visualization of the ducts is effective in locating the offending neoplasm, as is evidenced by the following cases.

Papilloma.—Mrs. P. P., a housewife aged 44, entered the hospital because of a "bleeding breast." Six weeks previously, while adjusting her brassiere, she observed a serosanguineous secretion escaping from the left nipple. This was

4. Stowers, J. E.: Significance of Bleeding or Discharge from the Nipple, Surg., Gynec. & Obst. **61**:537, 1935.

5. Adair, F. E.: Sanguineous Discharge from the Nipple and Its Significance in Relation to Cancer of the Breast, Ann. Surg. **91**:197, 1930.

6. Tapie, Pierre: The Bleeding Nipple, M. J. & Rec. **121**:537 (May 6) 1925.

7. Greenough, R. B., and Simmons, C.: Papillary-Cystadenomata of the Breast, Ann. Surg. **45**:188, 1907.

8. Miller, E. M., and Lewis, Dean: The Significance of a Sero-Hemorrhagic or Hemorrhagic Discharge from the Nipple, J. A. M. A. **81**:1651 (Nov. 17) 1923.

9. Cheatle, G. L., and Cutler, Max: Tumors of the Breast: Their Pathology, Symptoms, Diagnosis and Treatment, London, Edward Arnold & Co. 1931. Cutler.[1]

10. von Saar, G.: Ueber Cystadenoma mammae und Mastitis chronica cystica, Arch. f. klin. Chir. **84**:223, 1907.

11. Lewis, Dean, and Geschickter, C. F.: Ovarian Hormones in Relation to Chronic Cystic Mastitis, Am. J. Surg. **24**:280, 1934.

12. Hirschberg, A.: Ueber die vikarüerende bzw. komplementäre Menstruation, Centralbl. f. Gynäk. **38**:929, 1914.

repeated daily. There were no pains, tenderness or history of trauma. She had successfully nursed each of her three children, the youngest of whom was 2 years of age.

The breasts were small, atrophic and soft. There were no points of localized tenderness such as are sometimes seen with a papilloma, and no tumor could be palpated. Several subareolar milk ducts were dilated, and on compression two drops of bright red blood escaped from one centrally placed duct and a serous secretion escaped from its neighbors. Transillumination and soft tissue roentgenograms failed to locate the pathogenic lesion.

A hemorrhagic discharge was the only presenting symptom, and no abnormal physical signs could be found. In all probability a papilloma of the milk ducts

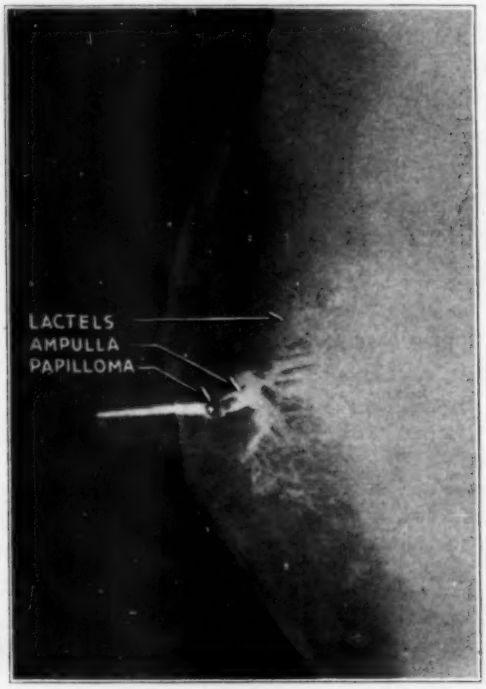

Fig. 1.—Mammogram in a case of papilloma, showing the bleeding duct visualized by the injection of 2 cc. of colloidal thorium dioxide. The papilloma appears as a "negative shadow" in the ampulla.

was the causative lesion, but such a diagnosis was entirely conjectural. In order to obtain definite information, mammographic visualization was employed. The bleeding duct was cannulated with a blunt no. 26 gage needle, and 2 cc. of colloidal thorium dioxide was introduced. The stereoscopic roentgenograms gave an accurate pattern of the ducts in the diseased lobule. The nipple portion of the duct was smooth, regular and of uniform diameter, but the ampullar segment contained a "negative shadow" or "filling defect." This was interpreted by Dr. H. B. Hunt as being a pedunculated tumor which protruded into the ductal lumen and displaced the contrast medium (fig. 1). The ramifying lacteal ducts and acini were

clearly visualized and presented a normal pattern. The hemorrhagic discharge, the absence of a palpable tumor and the roentgenographic silhouette of a localized, noninfiltrating, pedunculated neoplasm arising from the wall of a lactiferous duct characterized this tumor as being a benign papilloma (fig. 2).

Because the neoplasm was situated near the base of the nipple, making it technically impossible to excise the diseased lobule without injuring the neighboring duct, simple mastectomy was performed. Macroscopic examination demonstrated a papilloma the size of a pea arising from the wall of the duct. At the

Fig. 2.—Photomicrograph of the offending papilloma.

tip of one of the papilliferous projections a small bleeding point was seen, which accounted for the hemorrhagic discharge. Morphologically, the tumor was classified as a benign papilloma.

The mammographic studies accurately located the offending tumor and so clearly revealed its identifying characteristics that the correct diagnosis was made preoperatively. Such results are not fortuitous, for in six other instances definite contrast silhouettes of the provocative papillomas were obtained by stereoscopic mammograms.

Carcinoma.—Mrs. K. K., a housewife aged 38, was worried about a lump in her breast associated with a bloody discharge from the nipple. After the birth of

her baby, now 18 months old, a "caked breast" developed. The soreness soon subsided, but the hard, firm mass persisted and steadily increased in size. Three months before the present examination a serohemorrhagic discharge escaped from the right nipple.

Examination disclosed a firm, fixed tumor mass occupying the upper outer quadrant of the right breast. A bloody discharge was escaping from one centrally placed duct and a clear serous fluid from several of its contiguous mates. The tumor mass was not translucent but cast a hazy indefinite shadow. The right axilla contained several small, hard, discrete lymph nodes. Clinically, this appeared to be an advanced carcinoma which had metastasized to the regional lymph glands. In order to see what changes had taken place in the respective lactiferous ducts, a mammogram was made. The bleeding orifice was cannulated and 2 cc. colloidal thorium dioxide was injected into it. The roentgenographic

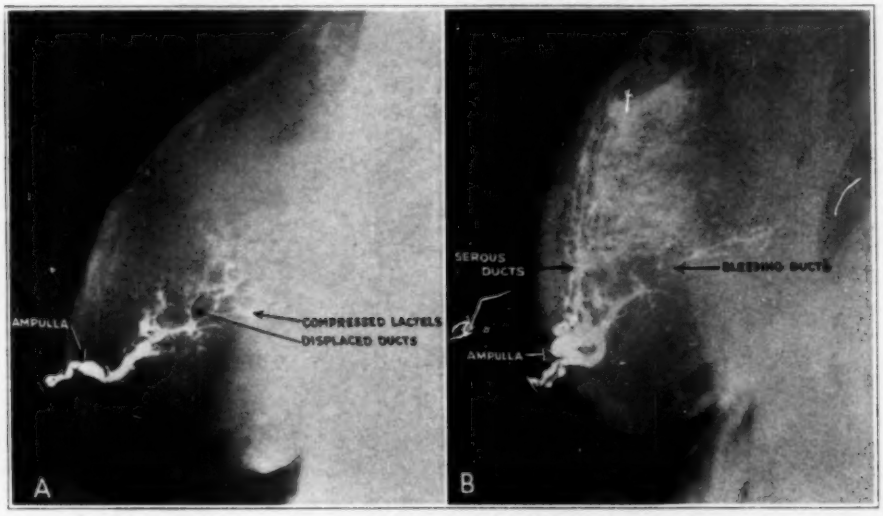

Fig. 3.—Mammograms in a case of carcinoma. *A* shows a bleeding duct into which 2 cc. of colloidal thorium dioxide was injected. The outer segment of the duct is smooth, tortuous and dilated; the inner portion has but few communicating ducts, for they have been destroyed, displaced and compressed by the malignant tumor. *B* shows a duct emitting a serous secretion. Colloidal thorium dioxide was used for the medium. The same destructive process is present as was observed in the bleeding duct, but it is not so far advanced.

silhouette showed the outer segment of the duct to be normal, but the tumorous portion resembled a filamentous cobweb (fig. 3 *A*). Not only had the infiltrating neoplasm invaded the ducts and thus reduced the size of their lumens, but the rapidly growing malignant cells had distorted, displaced and even destroyed a number of communicating radicals. Hence, the hemorrhagic discharge was produced by a destructive, invasive degenerating type of tumor.

The difference between the duct pattern of a papilloma and an invasive carcinoma is so striking that one has no difficulty in determining the cause of the bloody discharge.

SEROUS DISCHARGE

Patients have a tendency to consider a serous discharge from the nipple as being inconsequential, when in reality it may be associated with a grave pathologic condition. Gross [13] reported that a thin, watery, straw-colored fluid escapes from the breast in 10 per cent of all cases of sarcoma. Stowers [4] pointed out that a unilateral serous secretion frequently accompanies a mild infection of the lactiferous ducts. Deaver and McFarland [14] found that 25 per cent of their patients with intracystic papilloma complained of such a discharge. Adair [5] maintained that a watery serous fluid is frequently associated with a carcinomatous neoplasm. In our experience a carcinoma does not give rise to any pathognomonic discharge. At first the secretion may be serous, but as the tumor undergoes degenerative changes it may become hemorrhagic. Likewise, a mammary cancer may emit a serosanguineous discharge from one duct and a clear serous secretion from its neighbors.

It is obvious that a person complaining of a spontaneous emission of serum from the nipple has ample cause to worry. Every possible diagnostic procedure should be employed until an accurate diagnosis can be made. The following cases demonstrate that mammographic visualization of the discharging milk ducts give valuable information concerning the pathogenesis of the abnormal secretions.

Cancer with a Serous Discharge.—In the second case reported a frank hemorrhagic discharge escaped from one centrally placed duct and serous fluid from the other. The mammogram of the bleeding duct showed an invasive carcinoma which had obstructed, displaced and destroyed the regional lacteal ducts. In order to visualize the pathologic process which was responsible for the serous secretion, a comparative mammogram was made by injecting 3 cc. of colloidal thorium dioxide into one of these ducts. The same characteristic deformities were observed in the duct emitting the serous secretion as in its bleeding mate, but not to such a marked degree (fig. 3 *B*). Many of the smaller lacteal ducts were visible, less destruction had taken place and the degenerative process was not so advanced, for the duct into which the medium was injected occupied the periphery of the lesion where the vascular supply was intact.

This case clearly demonstrates that the nature of the escaping secretion may be altered as the pathologic condition pursues its evolutionary cycle.

Postlactation Involvement.—Mrs. L. McC., a housewife aged 28 years, had observed a bright bloody discharge from the right breast and a few drops of a clear serous fluid escaping from the left nipple. There was no pain, tenderness or abnormal sensation. She had nursed each of her four children, the youngest being 2 years of age. During each period of lactation she had produced large quantities of milk. In fact, the breasts had to be partially decompressed between nursing intervals in order to prevent the milk from spontaneously escaping from the ducts.

13. Gross, cited by Greenough and Simmons.[7]

14. Deaver, J. B., and McFarland, J.: The Breast: Its Anomalies, Its Diseases and Their Treatments, Philadelphia, P. Blakiston's Son & Co., 1917.

On examination, both breasts were found to be large, pendulous and firm. A stripping massage of the right nipple expressed bright red blood from one duct, while a serous secretion was expressed from six ducts of the left breast. The subareolar ducts were dilated, but no abnormalities were detected in either gland. The serous secretion was composed of a clear homogeneous fluid laden with degenerating epithelial cells, a few droplets of oil and an occasional leukocyte. No bacteria were present.

A contrast mammogram of the right breast demonstrated the presence of a bleeding papilloma. In order to ascertain the cause of the serous discharge from the left breast, thorium dioxide was introduced into the offending ducts. The stereoscopic mammogram gave a striking pattern of the entire ductal system. The

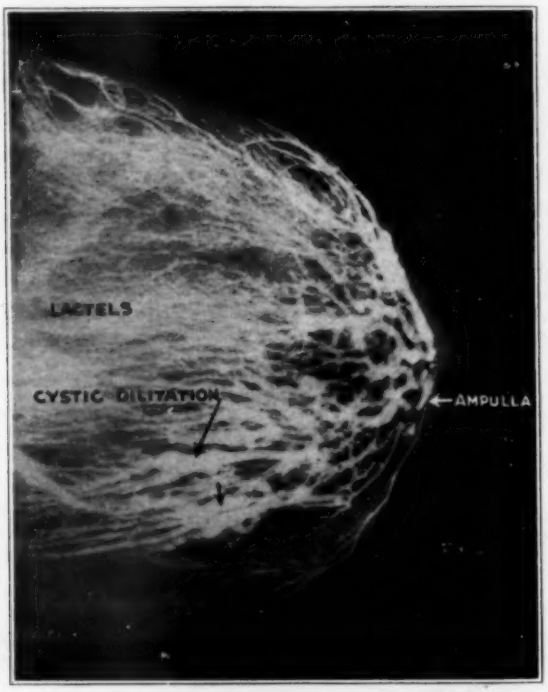

Fig. 4.—Mammogram of an involuting breast. Lipoiodine-Ciba (ethyl) diiodobrassidate) was injected into six ducts. Note the tortuous ampullae, the uniform dispersion of the ducts and the localized areas of ductal dilatation (normal involuting breast).

ducts ramified the matrix in an evenly distributed manner. The ampullae were dilated, and one or two had begun to undergo cystic degeneration. The achitectural arrangement of the smaller lacteal ducts and acini was normal, thus eliminating the presence of any neoplasm (fig. 4). Such a ductal pattern is characteristic of a multiparous gland in a state of secretory quiescence. The escaping serous fluid merely represents the products of desquamation from an enormous ductal system. In this particular case there was no evidence of an incipient malignant growth. Undoubtedly the slight localized dilatation of the ampullae was due to a retention of the desquamative products.

The right breast was excised because of the papillomatous growth, and the patient insisted that the left one be removed for cosmetic reasons. Macroscopic and histologic studies of the latter confirmed the mammographic diagnosis of postlactation involution.

The second and third cases emphasize the value of the visualization studies, for in one instance the serous discharge was associated with a carcinoma and in the other it was merely the normal response of the multiparous breast.

GREENISH WHITE DISCHARGE

Occasionally a patient desires to know the significance of a thick greenish white discharge which spontaneously escapes from the breast. Unfortunately, this symptom has no diagnostic significance but may be associated with a number of conditions, such as a desquamative cyst, an infected cyst or postlactation involution. The pathogenesis depends on the functional status of the breast, the type of lesion present, the age of the patient and the presence of infection. There is some question as to whether the bacteria, when present, irritate the epithelial lining of the ducts and accentuate the desquamative process or whether they are merely harmless saprophytes. The following cases are instructive.

Infected Cyst.—Mrs. G. G., a housewife aged 29, sought advice because of a bilateral mastalgia associated with a "pussy discharge" from the breast. She had been able to nurse each of her two children, the youngest of whom was 2½ years of age. Three months previously she first experienced distressing pains in both breasts, which were particularly annoying just preceding the menstrual flow. During the past month a thin whitish green discharge seeped from the right nipple, and the breast was so sore and tender that she was unable to wear her brassiere. Hot fomentations and energetic therapy with theelin proved ineffectual. Eight days before the present examination she discovered a hard, firm, tender lumph in the right axilla.

On examination both mammary glands were small and atrophic but extremely tender. The right breast was particularly painful. Several small, discrete tender nodules were scattered throughout both matrices. Gentle massage of the right nipple expressed a thick whitish fluid, which was laden with gram-positive diplococci, degenerating leukocytes and numerous epithelial cells. Both breasts were translucent, and roentgenograms did not demonstrate any abnormalities.

The whitish green discharge, the multiple nodules and the intense mastalgia suggested the diagnosis of cystic degeneration of the breast with coincidental infection. In order to obtain a visual concept of the altered ducts, a contrast mammogram was made. Colloidal thorium dioxide was injected into the orifices of the discharging lacteal ducts, and the resulting stereoroentgenogram presented an accurate reproduction of the diseased ducts. The ampullae were small and of a uniform diameter, and the ducts were evenly dispersed throughout the matrix. In one area a confluence of several ducts formed a large cyst (fig. 5). Its walls were smooth, and there was no evidence of an infiltrating or papillomatous tumor. When the cystic cavity was distended with thorium dioxide, it was definitely palpable and exquisitely tender. In other portions of the breast small cysts were just beginning to form, and the pathologic process seemed to involve the entire gland.

The mammogram clearly showed that the ducts were undergoing a cystic degeneration, and the nature of the escaping discharge indicated that the milk ducts and their cysts had become secondarily infected. These were not true retention cysts, for they still communicated with the regional ducts. Because such a process is not malignant, it was thought that conservative therapy, such as the application of hot fomentations, the administration of theelin and thyroid extract and general systemic stimulation, might give her some relief. This assumption was based on the fact that the cysts had adequate drainage through the patent ducts.

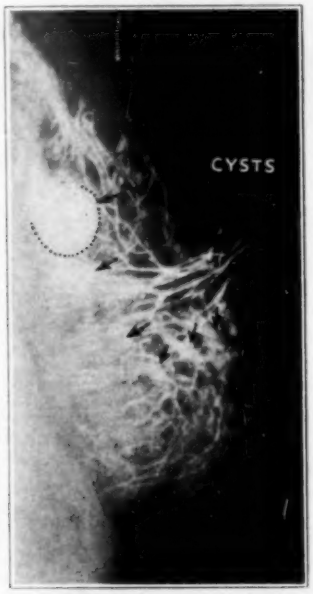

Fig. 5.—Mammogram in a case of multiple cysts. The large cyst as well as smaller cystic dilatations of the ducts are visualized by means of colloidal thorium dioxide. They all communicate with the regional ducts.

Postmenopausal Involution.—Mrs. A. S., a housewife aged 52, had complained of severe mastalgia for the past three months. The tantalizing pains were confined to the outer lower quadrant of the left mammary gland and were associated with a spontaneous greenish white discharge from the nipple. There was no history of trauma, and the patient had not menstruated for the past eighteen months.

Both mammary glands were extremely small, atrophic and involuted. There was practically no parenchymatous tissue, but situated in the lower outer quadrant of the left breast was a tense neoplasm the size of a walnut. It was movable and semifluctuant and when compressed a tenacious greenish white fluid which contained degenerating leukocytes, epithelial cells and gram-positive diplococci escaped from the nipple. The breasts were so closely apposed to the wall of the chest that transillumination and soft tissue roentgenograms were very unsatisfactory.

A mammographic pattern was obtained by cannulating the lactiferous ducts and distending them with colloidal thorium dioxide. In the outer lower quadrant several regional ducts became confluent and formed a large cystic cavity (fig. 6). This cyst was able to evacuate its contents through its communicating ducts, which accounted for the escaping secretion. The remaining ducts honeycombed the matrix in a uniform manner, presenting a normal architectural pattern. In certain areas the ampullae were slightly dilated, and small localized cysts were formed.

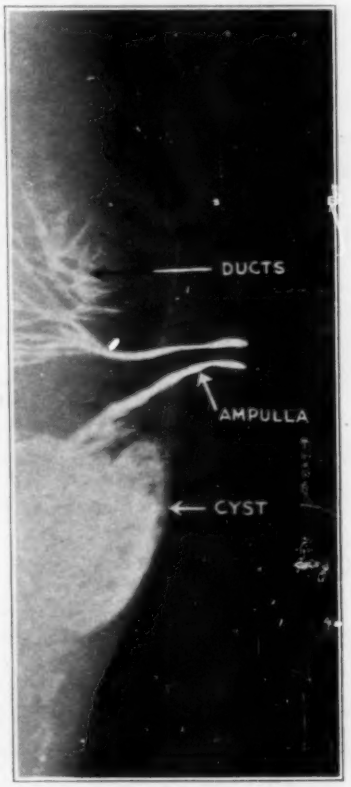

Fig. 6.—Mammogram in the case of an infected cyst. A large cyst which communicates with the ducts, thus accounting for the discharge, is visualized by means of colloidal thorium dioxide. The upper portion of the breast appears normal.

In this particular case the mammogram gave a clear concept of the disease process. The abnormal discharge originated within a small cyst and the involuting ducts. The mild secondary infection combined with the degenerative products of desquamation accounted for the characteristic greenish white color of the discharge. Radical therapy was not indicated, for such processes usually become quiescent after the menopausal balance has been established. The administration of thyro-ovarian extract and theelin and the application of moist heat usually suffice to control the immediate discomfort.

MILKY DISCHARGE

A milky discharge may occur in several conditions which prompt the patient to seek medical advice. Fortunately, a careful history and examination will usually divulge the pathogenic factors. Frequently such a discharge will seep from the nipples of the new-born, in which instance both breasts are hypertrophied, tense and tender. All symptoms subside spontaneously within two or three days. Occasionally a similar milky fluid escapes from virginal breasts during puberty. Postlactation involution is sometimes retarded, in which event there may be

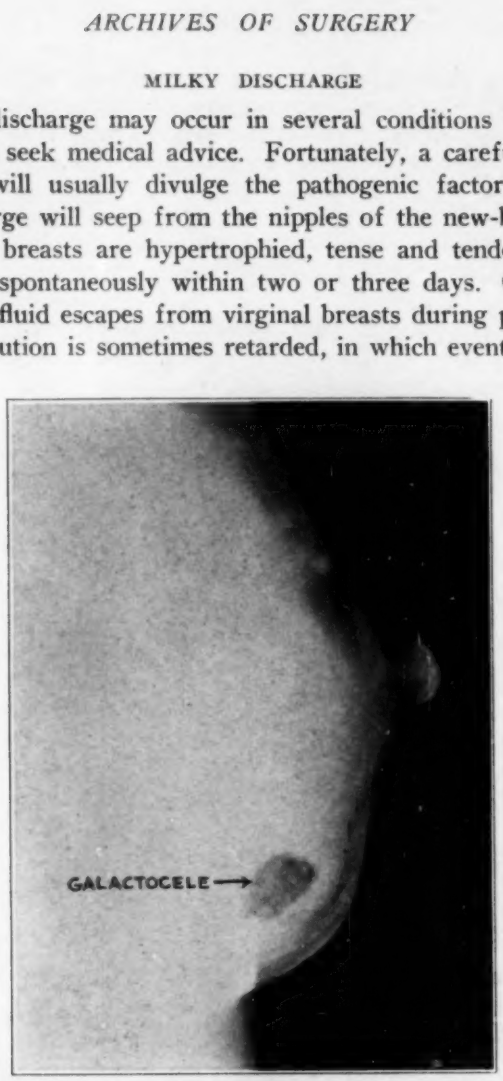

Fig. 7.—Mammogram in a case of galactocele. The inflated cyst has a smooth wall and does not communicate with the regional ducts.

a spontaneous leakage of milk for several months after active nursing has subsided. Sometimes a small neoplasm is discovered in an actively secreting breast, and it becomes imperative to know whether it is a galactocele, an adenofibroma, a retention cyst or a carcinoma. Contrast mammograms are valuable in determining the exact status of the ducts and the secretory system.

Galactocele.—Mrs. A. M., a housewife aged 26, observed a painful "lump" in the lower part of the left breast about one month prior to the birth of her last baby, now 10 days old. On the third postpartum day, synchronous with the flow of milk, the mass more than quadrupled its size. Nursing or evacuation of the breast did not reduce the size of the intumescence.

A small encapsulated tumor the size of a walnut was palpable in the outer lower quadrant of the left breast. The neoplasm was not semifluctuant and did not transmit light. Milk could be expressed from several ducts, but no abnormal secretions were detected. Compression of the tumor did not augment the discharge or decrease the size of the mass.

In order to ascertain the exact nature of this midmammary neoplasm, an insufflation mammogram was made. An exploring needle was inserted directly into the tumor mass, 10 cc. of viscid milky secretion was aspirated and the cyst was distended with an equal volume of air. The walls of the inflated cyst were distinctly outlined, and there were no patent communications with the regional ducts (fig. 7). Such characteristics were pathognomonic of a sequestrated galactocele.

Fig. 8.—Mammogram of an engorged breast. There is enormous dilation of the ampulla and communicating ducts due to a retention of secretions.

In this particular case an accurate diagnosis was made without mutilating the lactating breast by taking biopsy specimens, and conservative treatment was instituted with no fear of causing undesirable complications.

Retention Engorgement of the Breast.—Mrs. R., a 26 year old housewife, entered the hospital complaining of "caked breasts." She had been well until two days prior to admission, at which time she decided to wean her 8 month old baby. In spite of the fact that she produced a copious supply of milk, she refused to nurse the child and would not permit the breasts to be decompressed by a pump. The mammary glands became large, swollen and very tender. A milky

discharge seeped from the nipples, and for twelve hours she suffered excruciating pains, nausea, headaches and fever.

Both breasts were more than three times their regular size, and they were flushed, tense and exquisitely tender. Milk was escaping from several ducts of each nipple. The patient was very ill, with a temperature of 103.6 F. and a leukocyte count of 23,000.

It was apparent that the engorgement of her breasts was due to a retention of milk, but the intense pains, the febrile response and the leukocytosis suggested acute mastitis. An accurate visual concept of the disease process was obtained by mammographic studies. One of the seeping ducts was cannulated with a blunt

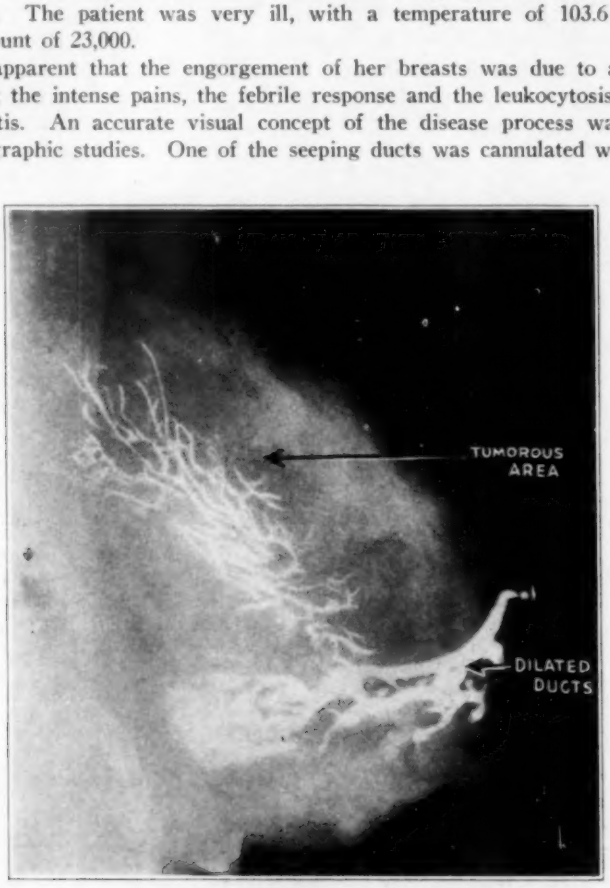

Fig. 9.—Mammogram in a case of "caked breast." The main duct is dilated, its walls are smooth and the communicating branches are large. In the tumorous area the ducts are small and compressed, but there is no evidence of localized invasion or destruction. The diagnosis was localized mastitis.

no. 25 gage needle, but no thorium dioxide could be introduced without augmenting the intense pain. Apparently the ducts were so dilated with retained secretions that they were unable to accommodate the contrast fluid. A large quantity of viscid milk was aspirated from each breast by means of a pump, and both glands became soft and compressible. Fifteen cubic centimeters of colloidal thorium dioxide was injected into a centrally located duct in each breast. The mammographic silhouette demonstrated an enormously dilated ampulla and tributaries, but otherwise the pattern was normal (fig. 8). The intense mastalgia, the turgidity of the breast and the systemic responses were all caused by retention of normal secretions and not by a coincidental mastitis.

"Caked Breast."—Mrs. D., a 16 year old girl, gave birth to a baby who was sent to a foundlings' home. She never nursed the infant, and both breasts were permitted to undergo postpartum involution. During the first three days she complained of a mild mastalgia; from the fifth to the eighth day both breasts were swollen, engorged and painful; by the thirteenth day they were soft and pliable, except for one small indurated area in the upper outer quadrant of the left gland. Pressure on this tumor mass expressed a yellowish white material from one duct, while a clear milky secretion escaped from the others. In order to obtain a visual concept of the changes in the ducts, a mammogram was made.

Six cubic centimeters of colloidal thorium dioxide was injected into the duct which emitted the yellowish secretion, for it presumably drained both the tumorous and the normal portion of the breast. The segment of the visualized duct traversing the normal breast tissue appeared smooth and moderately dilated but otherwise normal, while the ramifying lacteal ducts which penetrated the indurated area were small, compressed and displaced (fig. 9). There was no evidence of destruction or invasion, which eliminated the possibility of a malignant process. The reduction in the size of the lacteal ducts was caused by a periductal inflammation and by retention of ductal secretions. The escaping yellowish discharge was composed of the products of inflammation and degenerating secretions which originated in the indurated or "caked" area.

COMMENT

A spontaneous emission of secretion from a nonlactating breast signifies an abnormal physiologic or pathologic condition. While such a symptom constitutes a definite warning, which should always be heeded, it must not be considered dangerous until so proved. Many unnecessary mastectomies have been performed for papillomas, serous cysts, galactoceles, postlactation involution, desquamative epithelial hyperplasia and chronic infections of the milk ducts just because such conditions provoked a discharge from the nipple. On the other hand, the dismissal of such symptoms as inconsequential may permit a benign lesion to undergo malignant transformation. Any physician, therefore, who assumes the responsibility of the management of lesions of the breast must be able to interpret the presenting signs and symptoms correctly. He cannot shift this diagnostic responsibility to the shoulders of the pathologist but must carry his own burden.

Contrast mammograms have proved invaluable in the recognition of mammary diseases. The true character of the offending lesion is clearly portrayed, and in addition the extent of the disease process is accurately determined. Such information is invaluable in aiding the surgeon to select the proper corrective procedure. If the mammogram demonstrates that the bloody discharge is being produced by a small isolated papilloma, excision of the tumor is curative. If, however, there are multiple papillomas, mastectomy is indicated. Likewise, if the stereomammogram demonstrates that the serous secretion originates from a simple cyst, conservative therapy may be employed, but if it reveals the presence of a carcinoma, radical measures are imperative.

The cases presented here were selected from a group in which three hundred and seventy-five mammographic studies were made. Experience indicates that the mammogram plays just as important a rôle in the diagnosis and treatment of lesions of the breast as does the pyelogram and the encephalogram in the recognition and treatment of disorders of the genito-urinary tract and the brain. Although the subject of mammography is still in its infancy, it holds forth promises of developing into an exact science. Additional experience and refinement of technic will add much to its value.

No mention has been made of the technic, indications and contraindications or complications after the injection of the ducts or insufflations of the breast, as these subjects have been treated adequately elsewhere.

SUMMARY

A spontaneous discharge from the nipple of a nonlactating breast is indicative of a physiologic or pathologic abnormality, but it furnishes no clue as to the provocative factor.

An abnormal discharge from the nipple means that the causative lesion has originated within or has secondarily invaded the ductal and secretory system of the breast.

A hemorrhagic, serosanguineous or serous discharge is not pathognomonic of any disease but may be associated with a papilloma, a carcinoma, a sarcoma or a simple cyst.

A serous, a greenish white, a purulent or a milky discharge may be symptomatic of desquamative epithelial hyperplasia, postlactation involution, "caked breast," retention mastitis, infection of the milk ducts, cysts or galactoceles.

A method of obtaining an accurate roentgenographic pattern of diseased or normal milk ducts has been developed. It consists of cannulating the orifices of the ducts with a blunt no. 26 gage needle and then distending them with contrast mediums, after which a stereoscopic roentgenogram is made. Any pathologic condition which destroys, invades, obstructs or distorts the ducts can be readily detected.

These visualizing mammograms are invaluable in determining the location, extent and identifying characteristics of pathologic states which produce abnormal discharge from the nipple. Typical mammograms demonstrating a papilloma, a carcinoma, a simple cyst, an infected cyst, retention mastitis, "caked breast," a galactocele and postlactation involution are presented.

The preoperative visualization of the breast permits an accurate diagnosis and the employment of the proper remedial measures. The need for biopsy and prophylactic mastectomy will be reduced to a minimum.

527 Medical Arts Building.

DOES OPERATIVE FUSION OF TUBERCULOUS JOINTS PRODUCE TUBERCULOUS MENINGITIS?

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Patients with tuberculosis of the joints often die of miliary tuberculosis, the most serious form of which is tuberculous meningitis. This is a problem that has long been troublesome to those who treat tuberculosis of the joints. Regardless of whether the patient is treated by conservative or by radical procedures, there is a certain mortality due to tuberculous meningitis. It is important, therefore, to attempt to determine which of the two phases of treatment of tuberculous joints allows the lowest mortality so far as tuberculous meningitis is concerned.

The records of the New York Orthopaedic Dispensary and Hospital lend themselves ideally to such a study because both the conservative and the radical treatment of tuberculosis of the joints have been given long trials at this institution.

For over forty years, or from the founding of the hospital in 1866 until 1911, tuberculosis of the joints was treated conservatively. A country hospital was opened in 1904 at White Plains, N. Y., where such patients could be treated by rest in bed, splints, casts and braces and where pure air, sunshine and good food were available.

The era of so-called radical treatment, of operative procedures for the purpose of eliminating all motion in tuberculous joints, had its inception at this hospital on Jan. 9, 1911. At that time, the first operative fusion for tuberculosis was performed by Dr. Russell A. Hibbs, for tuberculosis of the second and third lumbar vertebrae in a boy 9 years old. And for the twenty-five years since that time, operative fusion for all joints affected by the tubercle bacillus has been carried out in this institution. A comparative study, therefore, of the incidence of tuberculous meningitis following conservative treatment of tuberculosis of the joints with that following operative treatment can be made.

Disagreement exists as to whether operation on a tuberculous joint will or will not disseminate the disease and produce tuberculous meningitis. Many surgeons who definitely believe that fusion of tuberculous joints cures the tuberculosis state that the risk of producing meningitis thereby forces them to treat conservatively all patients with tuberculous joints. This factor alone seems to have cast certain disrepute on opera-

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tive fusion of joints for tuberculosis, especially when children are involved.

1. Does surgical intervention, therefore, produce tuberculous meningitis?

2. Does fusion of tuberculous joints decrease the mortality due to tuberculous meningitis?

With these questions in mind, the deaths due to tuberculous meningitis prior to the advent of operative fusion were investigated, recorded and compared with such fatalities since operative fusion was instituted. The date selected as the dividing line was 1912, since this was near the middle of the period during which the conservative treatment of tuberculosis of the joints was discontinued at the New York Orthopaedic Dispensary and Hospital. Therefore, the time from 1912 to 1935 was considered as the period of operative treatment of tuberculosis of the joints as against an equivalent length of time, from 1889 to 1912, which was designated as the period of conservative treatment.

TABLE 1.—*Incidence of Tuberculous Meningitis Before and After Operative Treatment of Tuberculosis of the Joints*

	1889-1912	1912-1935
No. of patients with tuberculosis admitted to the hospital	1,398	1,752
No. of operations, other than aspiration, performed on tuberculous patients	0	1,941
No. of deaths due to tuberculous meningitis	149	23
Percentage of deaths due to tuberculous meningitis in patients with tuberculosis	10.6	1.3

During the twenty-three year period before operative fusions came into use, when all tuberculous patients were treated conservatively, 1,398 persons with tuberculosis were admitted to the hospital, on whom no operations other than aspiration were performed. However, 149, or 10.6 per cent, of these patients died of tuberculous meningitis, making an average of 6½ deaths per year.

During a similar length of time when operative fusion was performed, there were 1,752 patients with tuberculosis admitted to the hospital, on whom 1,941 operations were performed. Only 23 of these patients, however, died of tuberculous meningitis. This is a percentage of 1.3 for patients admitted and 1.1 for operations performed, with an average of 1 death per year.

It should be stated here that 8 of the 23 deaths occurring between 1912 and 1935 were of patients on whom no operations had been performed because of their delicate condition at the time of admittance and during their stay in the hospital. If these 8 deaths were eliminated because of the fact that the patients were not operated on, the percentage of deaths for those patients who were operated on would drop from 1.1 to 0.77.

In all the 23 fatal cases, tuberculosis had been present in some form for from six months to seventeen years prior to the onset of tuberculous meningitis. The period that had elapsed between the date of operation and the onset of meningeal symptoms in the 15 patients who were operated on is given in table 2.

After studying table 2, it is difficult to state which deaths, if any, were directly due to operation. Each patient presented the true signs and symptoms of tuberculous meningitis, and none died of postoperative shock or other conditions extraneous to this discussion. The period necessary for tuberculous meningitis to develop and proceed to death is extremely variable. The duration of development is not known. It must be very inconstant if it parallels the length of time before death

TABLE 2.—*Length of Time from Operation to Onset of Meningeal Symptoms*

Length of Time	No. of Cases	Length of Time	No. of Cases
4, 9 and 10 days	3	5 months	2
4 weeks	2	8 months	3
6 weeks	1	12 months	1
9 weeks	1	16 months	1
4 months	1	No operations performed	8

TABLE 3.—*Postmortem Status of the Involved Joints*

No. of Cases	Status of Case	Status of Joint
1	Spinal fusion	Grossly solid
1	Spinal fusion	Definitely not solid
1	Sacro-iliac fusion	Definitely not solid
2	Tuberculosis of spine and hip associated	Spinal fusion solid; hip not operated on
4	No autopsy	Presence of fusion not known
6	Early death	Too early for fusion
8	No operation	No fusion

occurs after meningeal symptoms become evident, because death ensues rapidly in some patients, while others show a slow, steady decline after the appearance of the first sign of meningeal irritation.

Postmortem examinations were made on all but 4 of the 15 patients operated on. The diagnosis of tuberculous meningitis was confirmed in each case. Also a careful examination was made for the presence or absence of fusion. In only 1 patient was the fusion definitely solid—a patient with tuberculosis of the spine. In 2 patients a spinal fusion and a sacro-iliac fusion, respectively, were definitely not solid. In 2 patients who presented tuberculosis of the spine associated with tuberculosis of the hip, the spinal fusions were grossly solid; the hips were not operated on. Death occurred too early for fusion to have taken place in 6 patients. The status of the joint was not known for 4 patients on whom autopsy was not allowed, and it is obvious that fusion was not present in the 8 patients who had not been operated on.

In summary, in 1 case the fusion was solid, in 4 the status of the joint was not known and in 18 fusion was not present. This, therefore,

is evidence that lack of either operative or natural fusion of a tuberculous joint is in many cases a predisposing factor to tuberculous meningitis.

COMMENT

There might be criticism from several standpoints of the statistics presented herein. It might be said, for instance, that the diagnoses may not have been as accurate in the nineties as they are today, i. e., that perhaps tuberculous meningitis was not always diagnosed or was diagnosed erroneously. But from such reasoning it might be said, also, that perhaps tuberculosis of the joints was not always diagnosed accurately either. "Hip joint disease" treated as tuberculosis may not have been tuberculosis, for were not many of these cases in which cure was effected in that period really cases of coxa plana, slipping of the upper epiphysis of the femur and other conditions not caused by acid-fast bacilli. Osteomyelitis of the spine was rarely, if ever, differentiated from tuberculosis of the spine. In cases of the former tuberculous meningitis naturally would not be expected to develop, yet the condition might have been considered tuberculosis of the joints. Therefore, if the diagnoses were more inaccurate in the nineties than they are today, the error may favor equally the two sides of the question of tuberculous meningitis following tuberculosis of the joints.

It should be noted, however, that the patients treated during the conservative era were hospitalized for a longer period than those treated by operation, because the time required for treatment of tuberculosis of the joints is much greater when such joints are treated wholly by rest than when they are treated by operative fusion. The point might be raised, therefore, that the incidence of tuberculous meningitis would be greater in hospitalized patients observed for a long period than in those observed for a shorter period, because there would be more time during which tuberculous meningitis might develop. This factor being admitted, it would be fair to assume that the mortality percentage would be decreased no more than one-half. The figures then would be 5.3 per cent deaths instead of 10.6 per cent in patients not operated on, as opposed to about 1 per cent in patients operated on. However, this would still leave the mortality rate five times greater for nonoperative treatment than for operative treatment.

In fact, even if one carries the point so far as to consider the number of deaths as being equal for each twenty-three year period, there still is no evidence for the theory that to operate on a tuberculous joint incites tuberculous meningitis.

The answer, therefore, to the questions asked earlier seems to be: (1) that surgical intervention in a tuberculous joint does not produce tuberculous meningitis and (2) that fusion of tuberculous joints definitely decreases the mortality due to tuberculous meningitis.

CLINICAL AND EXPERIMENTAL OPERATIONS ON THE GALLBLADDER AND COMMON DUCT

RESULTS OF PRIMARY SUTURE

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Further progress in surgery of the biliary tract must depend on a reduction in mortality and morbidity, on a reasonable certainty of obtaining relief with a preservation of the maximum function and on a simplified technic, and must lead to earlier operation.

The first operation on the gallbladder has been credited to Fabricius,[1] who removed gallstones in 1618. Hulke[2] referred to a case reported about 1706 in which a stone was withdrawn from the gallbladder by a forceps. Petit[3] in 1743 reported a case in which stones were removed from a gallbladder which was incised when it was mistaken for an abscess, and the patient recovered. Thudichum[4] in 1859 proposed the removal of stones by drainage in two stages.

The first operation on the gallbladder in one stage was performed in 1867 by Bobbs[5] when he removed many gallstones and closed the incision by primary suture. The patient had occasional attacks of distress due to an overlooked stone in the cystic duct, but otherwise he had good health for over thirty-two years.

Early in 1878 Brown[6] explored a distended gallbladder without opening it. Spontaneous rupture and biliary drainage followed the freeing of adhesions, and the patient recovered.

Presented before the Chicago Surgical Society, March 6, 1936.

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2. Hulke, in discussion on Bryant.[10]

3. Petit, 1743, cited by Power, D'Arcy: Gallstones: A Plea for Earlier Operation, Brit. J. Surg. **1**:21, 1913.

4. Thudichum, J. L.: On the Pathology and Treatment of Gall Stones, Lancet **2**:421, 1859; cited by Brown.[6]

5. Bobbs, John S.: Case of Lithotomy of the Gall-Bladder, Tr. Indiana M. Soc. **18**:68, 1868. Brayton, A. W.: John S. Bobbs, of Indianapolis, the Father of Cholecystotomy, Indiana M. J. **24**:20 (July) 1905.

6. Brown, George: On the Treatment of Dropsy of the Gallbladder by Operation with Notes of a Successful Case, Brit. M. J. **2**:916 (Dec. 21) 1878.

Kocher [7] performed the first successful drainage of the gallbladder in June 1878. Sims [8] and Keen [9] shortly afterward drained the gallbladder, but their patients died. In 1879 Bryant [10] and Tait [11] reported successful drainage operations. The first successful cholecystectomy was performed by Langenbuch [12] on July 15, 1882.

Cholecystotomy with primary suture was used by Meredith [13] in 1883. This method was advocated by Rutherford Morison [14] when the gallbladder appeared to be in good condition, without infection or obstruction of the ducts by stones, and was used by many surgeons with good results.[15] However, Robson reported a fatal bile leak, and Kocher observed occasional recurrence of gallstones. Courvoisier,[16] Kocher and others at first anchored the sutured gallbladder to the abdominal wall, and a few sutured the wound extraperitoneally (Brockbank [17]).

Unfortunately, in this pioneer period primary suture was used by Deaver and others [18] in cases in which the cystic duct was obstructed

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7. Kocher, cited by Judd, E. S.; McIndoe, and Marshall, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1934, vol. 7.

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11. Tait, Lawson: Cholecystotomy Performed for Dropsy of the Gallbladder Due to Impaction of a Gallstone, Brit. M. J. **2**:778 (Nov. 15) 1879.

12. Langenbuch, C.: Ein Fall von Exstirpation der Gallenblase wegen chronischer Cholelithiasis, Berl. klin. Wchnschr. **19**:725, 1882.

13. Meredith, cited by Moynihan, B. G. A.: Abdominal Operations, Philadelphia, W. B. Saunders Company, 1915, vol. 2, p. 275.

14. Morison, Rutherford: Surgical Contributions from 1881 to 1916, Baltimore, William Wood & Company, 1916, vol. 2.

15. Marcy, H. O., in discussion on Richardson, M. H.: The Importance of Early Operation in Gall-Stones, J. A. M. A. **35**:1397 (Dec. 1) 1900. Pick, T. P.: A Case of Cholecystotomy, Internat. Clin. **3**:188, 1895. Meyer, W.: Ideal Cholecystotomy (Koenig's Incision), Ann. Surg. **58**:694, 1913. Robson, A. W. Mayo: Diseases of Gallbladder and Bile Ducts, ed. 3, Baltimore, William Wood & Company, 1904; Two Successful Cases of Cholecystotomy, with Results, Brit. M. J. **2**:833 (Oct. 31) 1885. Wells, Spencer, cited by DaCosta, J. C.: Modern Surgery, ed. 9, Philadelphia, W. B. Saunders Company, 1925, p. 1110. Kocher, quoted by Bickham, W. S.: Operative Surgery, Philadelphia, W. B. Saunders Company, 1924, vol. 4, p. 508.

16. Courvoisier, cited by Bickham, W. S.: Operative Surgery, Philadelphia, W. B. Saunders Company, 1924, vol. 4, p. 508.

17. Brockbank, E. M.: On Gallstones or Cholelithiasis, Philadelphia, P. Blakiston's Son & Co., 1896.

18. Deaver, J. B.: Cases of Cholecystotomy, Ann. Surg. **44**:61, 1896. Musser, J. H., and Keen, W. W.: Cholecystotomy, Am. J. M. Sc. **88**:333 (Oct.) 1884.

and in acute and chronic conditions in which either drainage or removal of the gallbladder should have been done.

The two stage operation in which the gallbladder was first sutured to the abdominal wall and later drained was tried by Halsted [19] and others, who promptly abandoned it for the single stage drainage operation. At first the drained gallbladder was sutured to the abdominal wall (Tait), but biliary fistula resulted frequently; the results were much better when it was not fixed to the wound (Robson).

Drainage of the gallbladder rapidly became the procedure of choice,[20] because most of the patients coming to operation had extensive changes in the biliary tract or liver with infection or jaundice. In recent years, owing to the increase in the frequency of operations for chronic conditions, the disadvantages of a biliary fistula (Ravdin [21]) and the large number of secondary operations after drainage, cholecystectomy has become the usual operation of choice (Palmer [22] and Bunts [23]).

Lack of roentgenographic visualization as a final test of function rather than pathologic changes in the liver and gallbladder have become only too frequently the indication for routine removal of the gallbladder. With slight alterations in the gallbladder and even after drainage or anastomosis, diminished visualization gives no final index of later function nor a true index of present tonus, elastic recoil (Copher, Kodama and Graham [24]) or contractile power (Ivy [25]).

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19. Halsted, cited by Bloodgood, J. C.: Halsted Thirty-Six Years Ago, Am. J. Surg. **14**:89 (Oct.) 1931.

20. Ochsner, A. J.: Technique of Gall-Bladder Operations, Surg., Gynec. & Obst. **2**:204 (Feb.) 1906. Moynihan, B. G. A.: Abdominal Operations, Philadelphia, W. B. Saunders Company, 1914, vol. 2, p. 275. Mayo, W. J.: The Present Status of Surgery of the Gallbladder and Bile Ducts, M. Rec. **63**:289 (Feb. 21) 1903; Surgery of the Gallbladder, Illinois M. J. **49**:303 (April) 1926; "Innocent" Gall-Stones a Myth, J. A. M. A. **56**:1021 (April 8) 1911. DaCosta, J. C.: Modern Surgery, ed. 9, Philadelphia, W. B. Saunders Company, 1925, p. 1034. Means, W. J., in discussion on Richardson, M. H.: The Importance of Early Operation in Gall-Stones, J. A. M. A. **35**:1397 (Dec. 1) 1900. Cheeseman, W. S.: Cholecystotomy, M. Rec. **44**:225 (Aug. 19) 1893.

21. Ravdin, I. S.: Drainage of Common Duct, S. Clin. North America **14**:127 (Feb.) 1934. Ravdin, I. S.; Riegel, C.; Johnston, C. G., and Morrison, P. J.: Studies in Biliary Tract Disease, J. A. M. A. **103**:1504 (Nov. 17) 1934.

22. Palmer, D. W.: The Rationale of Gallbladder Therapeusis, Ohio State M. J. **21**:309 (May) 1925.

23. Bunts, F. E.: Diagnosis and Surgical Treatment of Diseases of the Gall-Bladder, Ann. Surg. **82**:232 (Aug.) 1925.

24. Copher, G. H.; Kodama, S., and Graham, E. A.: Filling and Emptying of the Gall Bladder, J. Exper. Med. **44**:65 (July) 1926.

25. Ivy, A. C.: The Physiology of the Gall Bladder, Physiol. Rev. **14**:1 (Jan.) 1934.

The inflamed gallbladder may be visualized partially or not at all (Ivy and Bergh [26]), but whether the inflammation is primary or secondary to hepatitis cannot be demonstrated by a functional test. Clinical evidence has shown that this function may return after acute cholecystitis (Murphy and Bollman [27]). Ravdin and his co-workers found that bile salts could be completely absorbed from a damaged gallbladder.

Eusterman [28] pointed out that in about 10 per cent of cases the normal gallbladder gives a pathologic response, that is, a faint shadow or invisibility, which may be due to errors both in technic and in interpretation. He found a large group of cases in which there was positive cholecystograhpic evidence of disease but insufficient clinical symptoms or an absence of them.

Schmechel [29] reported relief after cholecystectomy in only 23.4 per cent of sixty patients in the absence of stones, while Graham and Mackey [30] observed relief in 60 per cent.

In routine removal of the gallbladder, especially in acute conditions, Stone and Owings [31] disregarded the greater safety of drainage, the possibility of a return of function and some of the well established technical and late complications of cholecystectomy. Several months after experimental cholecystectomy Ivy [25] observed the development of hepatitis. The dangers of ascending infection from an incompetent sphincter or from the formation of stones in the common duct may counterbalance the benefits of cholecystectomy.

Crump [32] found gallstones in 32.5 per cent of a thousand gallbladders at necropsy and cholesterosis in 36.8 per cent, making a total of 76.1 per cent of gallbladders with pathologic changes. There were stones in the ducts in 24 per cent, of which 60.2 per cent were at the papilla and 48.7 per cent in the cystic duct.

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26. Ivy, A. C., and Bergh, G. S.: The Applied Physiology of the Extrahepatic Biliary Tract, J. A. M. A. **103**:1500 (Nov. 17) 1934.

27. Murphy, G. T., and Bollman, J. L.: Concentrating Activity of Bile in Gallbladder Following Restoration from Acute Experimental Cholecystitis, S. Clin. North America **11**:917 (Aug.) 1931.

28. Eusterman, G. B.: Cholecystography: A Clinical Appraisal, Proc. Staff Meet., Mayo Clin. **2**:138 (June 22) 1927.

29. Schmechel, A.: Spätresultate operierter steinfreier Gallenblasen (Cholecystitis sine concremento), Zentralbl. f. Chir. **61**:673 (March 24) 1934.

30. Graham, E. A., and Mackey, W. A.: Consideration of Stoneless Gallbladder, J. A. M. A. **103**:1497 (Nov. 17) 1934.

31. Stone, H. B., and Owings, J. C.: The Acute Gallbladder as a Surgical Emergency, Ann. Surg. **98**:760 (Oct.) 1933.

32. Crump, C.: The Incidence of Gall Stones and Gall-Bladder Disease, Surg., Gynec. & Obst. **53**:447 (Oct.) 1931.

Drainage of the gallbladder has permitted the recovery of critically ill patients, frequently with a return of function. Halsted, Dieterich [33] and others observed that few of the badly damaged gallbladders which were drained gave rise to symptoms later, and only a few were reoperated on for stone in the common duct.

Chronic diseases of the heart, liver and kidney may become aggravated when cholecystectomy is done, and occasionally unexplained death follows. When function of the gallbladder exists, a sudden hepatic disturbance without previous compensatory changes may follow cholecystectomy (Cantarow, Gartman and Ricchiuti [34]).

The symptoms of disease of the gallbladder may be aggravated or actually begin (Case [35]) after an operation for drainage when normal or partial function is lost.

Rose [36] found on visualization of a series of gallbladders that of 801 with pathologic conditions 101 had normal function with stones, 161 poor function with stones, 209 faint filling, 90 delayed filling or emptying and only 240, or 30 per cent, no filling.

The function of the gallbladder after drainage has been carefully studied by visualization tests. In a series of twenty cases in which cholecystograms were made after cholecystostomy, Case found the gallbladder to be normal in three, while in eight there was a delayed or insufficient response, largely the result of adhesions, in seven stones were found and in two there was obstruction of the cystic duct. These findings were confirmed by reoperation.

Saint [37] found that the function of the gallbladder after drainage was impaired in eighteen cases, lost in eleven and good in seven. He reviewed the findings of others and concluded that drainage of the diseased gallbladder with the hope of a return of function was futile. He stated that he preferred removal in both acute and chronic conditions.

In recent years occasional reports by Willis,[38] Saint [37] and Sutherland [39] corroborate the merits of primary suture of the gallbladder after cholecystotomy in certain conditions.

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33. Dieterich, H.: Ergebnisse nach Cholecystostomie, Chirurg **5**:929 (Dec. 15) 1933.

34. Cantarow, A.; Gartman, E., and Ricchiuti, G.: Hepatic Function: Effect of Cholecystectomy on Hepatic Function, Arch. Surg. **30**:865 (May) 1935.

35. Case, J. T.: Personal communication to the author, Sept. 23, 1935.

36. Rose, C. B.: Cholecystography, S. Clin. North America **12**:1083 (Oct.) 1932.

37. Saint, J. H.: Late Results of Operations on Biliary Tract in Three Hundred Fifty-Nine Cases, Brit. J. Surg. **23**:299 (Oct.) 1935.

38. Willis, A. M.: Ideal Cholecystotomy, J. A. M. A. **78**:942 (April 1) 1922.

39. Sutherland, C. G., in discussion on Weir, J. F., and Snell, A. M.: Symptoms That Persist After Cholecystectomy, J. A. M. A. **105**:1093 (Oct. 5) 1935.

Restoration or preservation of the function of the gallbladder by primary suture has not been reported previously. The current belief is that function will be entirely lost, and the operation is never performed for the purpose of restoration (Judd and his co-workers [40]).

It is my belief that elderly patients or those who are poor risks will have less postoperative reaction with fewer hepatic and pulmonary complications and much better function after primary suture with cholecystotomy than after either drainage or removal. Improvement in cardiac condition has been noted clinically with a definite return toward normal after operations on the gallbladder (Fitz-Hugh and Wolferth [41]).

EXPERIMENTAL DATA

A series of experiments on dogs was planned to determine the early and late changes occurring in the gallbladder, bile ducts and liver. In all experiments primary closure of the abdomen was performed.

RESULTS OF INCISION OF GALLBLADDER WITH LIGATION OF CYSTIC DUCT

In nineteen experiments the gallbladder was split wide open from the fundus to the cystic duct with ligation of the cystic duct. In some of the experiments the cystic duct was permanently ligated with linen, while in others it was ligated with catgut, which usually permits the duct to open after from ten to fourteen days unless unnecessary trauma or heavy suture material is used.

In eleven of the experiments occlusion of the cystic duct was noted at postmortem examination. In six of these experiments, of from thirty-six to one hundred and fifteen days' duration, the cystic duct was ligated with linen and the gallbladder was split and left open. In five the cystic duct was ligated with catgut; in two there was obstruction on termination at the end of one week, while in three permanent occlusion resulted after from one to five months.

In two experiments after one week of occlusion of the cystic duct the gallbladder had reformed, except for a small area which was sealed by adhesions to the liver. In one experiment the gallbladder contained precipitated bile pigment with mucus.

In nine experiments in which there was occlusion of the cystic duct for from one to five months the gallbladder had entirely healed, and in two it was practically normal in size with a thin wall. In two experiments the gallbladder was enlarged; in one of these it had a thin wall and contained clear mucus with particles of bile pigment, and in the other it had an empyema with several small abscesses in the adjacent liver. In four experiments the gallbladder was contracted to from one-half to two-thirds its normal size. In the lumen of one gallbladder there was only thick mucus; in the lumen of two others a mass like coagulated mucus was found after one and five months, respectively, with bile stain in one, and in the lumen of the fourth gallbladder there was mucus with a

40. Judd, E. S.; McIndoe and Marshall, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1934, vol. 7.

41. Fitz-Hugh, T., and Wolferth, C. C.: Cardiac Improvement Following Gall-Bladder Surgery: Electro-Cardiographic Evidence in Cases with Associated Myocardial Disease, Ann. Surg. **101**:478 (Jan.) 1935.

gritty precipitate of bile. In one experiment the gallbladder was only about 1 cm. in diameter and contained a mass of laminated bile pigments with tarry bile and mucus.

There was bile pigment in five of the eleven gallbladders examined, or 45 per cent, although bile was removed and the cystic duct ligated completely in from one to fifteen weeks. In the experiments in which the cystic ducts were permanently obstructed no sand or precipitated bile was found in the common duct, although the duct was dilated in seven of the nine experiments which lasted over one week.

There were seven experiments of from one week to over four months' duration in which the gallbladder was split completely and the cystic duct was temporarily occluded by a catgut ligature. The catgut was absorbed in approximately from ten to fourteen days, with no stricture or scarring. In one experiment it was absorbed before the split gallbladder was closed, and when the acutely ill animal was killed after six days the gallbladder was found to be covered with a thick precipitate of bile, to show bile peritonitis but to contain no pus. In two other experiments precipitated bile pigment was found in the gallbladders. In one experiment (no. 74) bile sand was found in the gallbladder and the common duct after two weeks, and in another (no. 62) it was found only in the duct. Precipitated bile pigment was found in the gallbladders of 60 per cent of the animals in this group and somewhere in the biliary tract of 71 per cent.

The common duct was normal in four experiments and enlarged in three, with bile pigment in two, or 30 per cent.

RESULTS OF INTRAVENOUS INJECTION OF DYE

In five experiments sections of the gallbladder were examined after the intravenous injection into the dogs of from 0.08 to 0.25 Gm. of tetrabromophenolphthalein sodium per kilogram of body weight. In two experiments the gallbladder showed slight edema and increased round cell infiltration after from one to two weeks, but in two which were extended over three and six months the gallbladders were normal except for slight adhesions at the fundus where sections had been removed.

In seven experiments, after the intravenous injection of from 0.04 to 0.05 Gm. of tetraiodophenolphthalein per kilogram of body weight, sections of the gallbladder showed little or no change after one week. However, a few gross particles of bile pigments were found in the bile from the gallbladder in two experiments, and in a third (no. 53) a large amount of so-called sand was found at the end of one week, although no operation had been done on the gallbladder or abdomen. In a fourth experiment (no. 31), after a large piece of the gallbladder was removed for microscopic examination at the end of one week, the animal was permitted to live eight months. The gallbladder was about two-thirds normal size and largely functionless but contained no bile sand, while the common duct was considerably dilated and thickened and contained a large amount of bile pigment. The liver appeared to be normal. This makes precipitated bile pigment in the gallbladder in three, or 43 per cent of the experiments, one week after the intravenous injection of dye.

In about one third of these twelve experiments occasional areas of focal necrosis were found in the liver which contained polymorphonuclears, lymphocytes and a few fibroblasts. Sections taken several weeks later and also from numerous control animals did not show these changes.

One week after the intravenous injection of 0.04 or 0.05 Gm. of tetraiodophenolphthalein per kilogram of body weight into fourteen rabbits there were no changes in the gallbladder and liver.

Graham, Cole, Copher and Moore [42] concluded that the toxicity of this halogenated dye group was due to the phenolphthalein part of the molecule.

Acute degeneration of the liver in a patient after the giving of the dye clinically was reported by Dyas, Sheldon and Dyke.[43] A serious reaction was observed by Bailey [44] in a patient with jaundice. Visualization of the gallbladder should not be attempted during attacks of obstruction of the biliary tract, acute hepatitis or cholecystitis or after any period of starvation or illness.

The effect on the gallbladder of direct injection of varying concentrations of tetrabromophenolphthalein sodium was observed in seven experiments.

After intravenous injection, Copher observed that there was an average concentration of 0.2 per cent of bromine in the bile from the liver, while there was 0.6 per cent in that from the gallbladder, which did not excrete or absorb the dye to any extent.

RESULTS OF DIRECT INJECTION OF SOLUTIONS INTO THE GALLBLADDER AND COMMON DUCT

In two experiments 10 cc. of a 12.5 per cent solution of tetrabromophenolphthalein sodium was injected into the gallbladder without ligation of the cystic duct. There were edema and increased round cell infiltration one week later. After one hundred and fifty days there was no change except a slight adhesion at the site of the injection.

In three experiments a 12.5 per cent solution of tetrabromophenolphthalein sodium was injected into the gallbladder with ligation of the cystic duct with linen. After seven days there was marked distention with acute inflammation and necrosis of the wall of the gallbladder with turbid contents. Microscopically, there were edema, hemorrhagic areas, many round cells and extensive desquamation of the epithelium and definite hepatitis.

In another experiment after seventy-five days there was a nubbin gallbladder, 1 cm. in diameter, which contained a small mass of soft bile pigment and mucus, with marked fibrosis and an absence of epithelium.

In one experiment acute inflammation was found one week after injection of a 5 per cent solution of the dye into the gallbladder with ligation of the duct. Roentgenograms made after from three to seven days showed some absorption of the dye by the gallbladder.

In six experiments a 15 per cent solution of sodium iodide was injected into the gallbladder without ligation of the cystic duct. Four of these experiments were terminated in from four to eight days. In one the gallbladder was surrounded by adhesions and was somewhat contracted. There were edema and a slight increase in the round cells. The liver was normal. In two experiments at the end of one hundred and sixteen and one hundred and nineteen days there

42. Graham, E. A.; Cole, W. W.; Copher, J. H., and Moore, S.: Cholecystography: The Use of Phenoltetraiodophthalein, J. A. M. A. **86**:1899 (June 19) 1926.

43. Dyas, G. E.; Sheldon, J. H., and Dyke, S. C.: Death Coincident with Oral Administration of Sodium Tetraiodophenolphthalein, Brit. J. Radiol. **1**:75 (March) 1928.

44. Bailey, Hamilton: Emergency Surgery, ed. 2, Baltimore, William Wood & Company, 1936, p. 139.

were only slight adhesions about the site of injection, while cultures and sections from the gallbladder and liver were negative.

In one experiment two hundred and forty days after the injection of a 15 per cent solution of sodium iodide into the gallbladder with ligation of the cystic duct with linen there was marked contraction and fibrosis of the gallbladder to 1 cm. in diameter. It contained a small ball of mucus with some bile pigment. There was apparent progressive obliteration of the lumen nearly to the fundus. The common duct was moderately enlarged. The fibrotic changes were similar to those seen after the injection of a 12.5 per cent solution of tetrabromophenolphthalein sodium.

In two experiments a 15 per cent solution of sodium bromide was injected into the gallbladder without obstruction. After six days there were edema of the wall and a precipitated mass of bile pigment around the puncture wound. In one experiment no change was observed after ninety-five days.

In one experiment a 15 per cent solution of thorium nitrate was injected into the gallbladder without obstruction. After six days there were edema, increased round cell infiltration and a few polymorphonuclear cells. There was some congestion of the liver.

In one experiment physiologic solution of sodium chloride was injected into the gallbladder as a control, with no changes except a few adhesions at the site of injection after twenty days.

In many of the experiments cultures of the bile and liver were taken and found to be negative.

In thirteen experiments various solutions were injected into the gallbladder without ligation of the cystic duct. A deposit of pigment was found in only one gallbladder; this occurred at the site of the injection.

In six experiments the cystic duct was ligated permanently at the time of injection of the dye or sodium iodide into the gallbladder. Pigment was found in the gallbladder in two. There was no bile sand in the common duct in these nineteen experiments.

Some chemical inflammation of the gallbladder resulted, especially from the dye and the solutions of sodium bromide and thorium when the cystic duct was not ligated, but it quickly cleared. There was some congestion in the liver at the end of a week.

The cystic duct was ligated in three control experiments:

In one the cystic artery and duct were ligated with linen, and the neck of the gallbladder was crushed. One week later the gallbladder was moderately distended but was of a normal color. Microscopically, only slight changes were observed.

In one experiment seventy-five days after ligation of the cystic duct with linen the gallbladder was contracted to one-third normal size and contained thick mucus but no bile. There was moderate fibrosis of the wall. The cystic duct was dilated below the ligature. Cultures were negative.

In another experiment the cystic duct was ligated with plain catgut so that it would remain obstructed for only about ten days. After forty-nine days the gallbladder and the liver were normal with a patent cystic duct.

In one experiment the common duct was ligated, and 12 cc. of a 15 per cent solution of sodium iodide was injected into the gallbladder. Death occurred in three days. There were extensive icterus and evidence of a septic cholangeitis, with positive cultures. The gallbladder was filled with black concentrated bile with little gross change, although the ducts were dilated.

In a control experiment the common duct was cut and ligated. After five days the animal was in good condition with no evident icterus, but the gallbladder was

distended and filled with thick mushy bile. There was hyperplasia of the mucosa, and cultures of the gallbladder and liver were negative.

In one experiment the insertion of a small needle into a normal gallbladder for injection resulted in a leak, with fatal bile peritonitis. After this the site of the puncture was ligated with catgut, because silk was observed to cut through into the lumen of the gallbladder.

SUMMARY OF DATA

In most experiments in which a small section was removed from the fundus of the gallbladder for microscopic examination there were few adhesions. Occasionally after a large section was removed contraction and a dilated common duct resulted, indicating a functionless gallbladder.

In three, or 5.1 per cent, of the fifty-four experiments on dogs, bile pigment sand or crystals were present in the common duct: In experiment 74, after the gallbladder was split and temporary occlusion of the cystic duct produced, the experiment being terminated after fourteen days, there were masses of pigment in both the gallbladder and the common duct. In experiment 62, which was similar to experiment 74, the gallbladder was adherent, and there was bile sand in the common duct after four and one-half months. In experiment 31 the injection of dye intravenously was followed by the removal of a large section from a normal gallbladder eight months previously, and at necropsy the gallbladder was contracted moderately with normal bile, but the common duct was dilated and contained a large amount of black sand. Previously, I [45] reported gallstones in the common duct after experimental suture of the common duct.

In nineteen experiments, after permanent obstruction of the cystic duct by ligature and removal of all bile, some bile pigment was found in seven gallbladders, or 36 per cent. This could enter only through small anastomosing bile ducts to the liver or by secretion.

Several months after the injection of a concentrated solution of sodium iodide and dye with ligation of the cystic duct there were extensive fibrosis and a nubbin gallbladder. While after splitting the gallbladder or taking a specimen for biopsy adhesions resulted, there was no extensive fibrosis or contraction of the wall. Permanent obstruction of the cystic duct was followed by hydrops only once and infection once, with a small abscess in the adjacent liver.

There was no bile sand in the common duct when the cystic duct was obstructed, although it was dilated in 88 per cent of the experiments. This is suggestive that the sand in the common duct may be formed in the gallbladder after traumatic or chemical changes.

Bile sand was found in five of seven experiments in which the gallbladder was split and a temporary ligature applied to the cystic duct; it was in the reconstructed gallbladder of four and in the common duct of two.

After the intravenous injection of dye without operation, bile sand or crystals were found in the gallbladder in three of twelve experiments.

After the injection of various solutions into the gallbladder without obstruction in thirteen experiments, a precipitate of bile was found once at the site of ligation. Mild chemical cholecystitis was usually present. Sepsis occurred only after obstruction of the common duct.

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45. McWhorter, G. L.: New Methods of Anastomosis of the Common Bile Duct, Arch. Surg. **18**:117 (Jan.) 1929; Experimental Suture of the Common Bile Duct with New Methods of Anastomosis: Results After Two and One-Half Years, S. Clin. North America **12**:163 (Feb.) 1932.

In thirty-three experiments on dogs in which the cystic duct was patent at necropsy, bile sand was found in eight gallbladders, or 24 per cent. There was either trauma to the gallbladder by incision and puncture or some chemical disturbance after the intravenous injection of the dye. No changes occurred in rabbits.

In the absence of trauma, precipitation of bile may follow chemical changes or irritation of the biliary tract, with a disturbed secretion, absorption or impaired emptying mechanism.

DATA OF OTHER AUTHORS

Some of the changes observed in the gallbladder may be analogous to those found in the urinary bladder by Graves and Davidoff.[46] After the injection of hypertonic solutions of sodium bromide or chloride into the bladder, they found edema, thrombosis, multiple hemorrhages, surrounding fibrinous adhesions and paralysis of the muscle, but not after the injection of isotonic solutions or a 14.56 per cent solution of sodium iodide. Goldstein and Abeshouse[47] found a 12.5 per cent solution of sodium iodide irritating but less so than a solution of sodium bromide. Emmett[48] found sodium iodide irritating clinically in the presence of cystitis. Weld[49] found absorption of a 25 per cent solution of sodium bromide without irritation in the renal pelvis, but Braasch and Mann[50] found that with retention an abscess might result.

The frequency of edema in some of these experiments on the gallbladder with little microscopic evidence of cellular infiltration may be explained in the absence of infection by an effort of the blood to act as a fixing agent or diluent to the irritating agent (Aldrich[51]) with a collection of abnormally large amounts of fluid in the tissues. In the presence of edema, stasis of bile may easily result because of obstruction. The intravenous injection of diluted solution of sodium hypochlorite was followed by chemical inflammation of the gallbladder (Mann[52]), but formation of stones was not reported.

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46. Graves, R. C., and Davidoff, L. M.: The Choice of Pyelographic Mediums, J. A. M. A. **80**:168 (Jan. 20) 1923.

47. Goldstein, A. E., and Abeshouse, B. S.: Historical and Practical Consideration of Pyelographic Media, Am. J. Roentgenol. **33**:165 (Feb.) 1935.

48. Emmett, J. L.: Elliott Treatment of Chronic Urethritis of Women: Preliminary Report, Proc. Staff Meet., Mayo Clin. **10**:545 (Aug. 28) 1935.

49. Weld, E. H.: Renal Absorption with Particular Reference to Pyelographic Mediums, M. Clin. North America **3**:713 (Nov.) 1919; The Use of Sodium Bromid in Roentgenography, J. A. M. A. **71**:1111 (Oct. 5) 1918.

50. Braasch, W. F., and Mann, F. C.: Effect of Retention in the Kidney of Media Employed in Pyelography, Am. J. M. Sc. **152**:336 (Sept.) 1916.

51. Aldrich, C. A.: Clinical Course of Generalized Edema, with Suggestions as to Its Possible Function, J. A. M. A. **84**:481 (Feb. 14) 1925.

52. Mann, F. C.: Production by Chemical Means of a Specific Cholecystitis, Ann. Surg. **73**:54 (Jan.) 1921.

Carter [53] found that in patients with typical symptoms of a disturbance of the gallbladder whose filling and emptying times were normal and whose roentgenograms showed no positive or negative shadows of stones, enlargement of the gallbladder, which is a result of stasis, was an important sign and was frequently present when stones were found at operation.

In four experiments I observed marked enlargement of the gallbladder after one week's starvation with water alone or with dextrose and water. The type of diet previous to visualization may affect the size of the gallbladder.

CLINICAL APPLICATION OF EXPERIMENTAL DATA

There appears to be a tendency to the formation of stones with stasis after partial or complete loss of function of the gallbladder and after trauma and certain chemical changes in the bile. However, no stones were found in the gallbladder in many experiments in which careful removal of a small section of the fundus was followed by suture and only once at the site of ligation of a needle puncture wound with silk. A thickened scarred wall did not seem to predispose to stones, although an unhealed area did.

The common duct will dilate and assume a part of the missing function of the gallbladder if the terminal sphincter is competent. The rôle of stasis is important in the formation of stones and infection and is dependent to a large extent on changes occurring at the outlet of the gallbladder and the common duct. It is easily seen how even small bile crystals or sand may produce varying degrees of spasm, inflammation or stricture when caught in the folds of mucosa or the glandular crypts, shown by Dardinski [54] to exist in the papilla of the common duct.

Infection was not found in experiments in which precipitated gallstones were found.

Biliary stasis may result clinically from physiologic disturbances after irregular or selective eating and particularly during an illness with gastro-intestinal disturbances.

Factors of surgical importance are the relief of inflammation, the removal of stones or particles, the correction of stasis and the restoration of maximum function.

Gallstones may result from systemic biliary changes, stasis or infection or in some instances from a combination of these factors. Clinically, stones may persist in the bile ducts for years with only vague

53. Carter, R. F.: Enlargement of the Gallbladder, Ann. Surg. **102**:194 (Aug.) 1935.

54. Dardinski, V. J.: Anatomy of Major Duodenal Papilla of Man, with Special Reference to Its Musculature, J. Anat. **69**:469 (July) 1935.

disturbances until acute obstruction or infection occurs. In the majority of patients stasis or intermittent obstruction with gallstones usually results in fibrosis and chronic inflammation with some impairment of function and the absence of roentgenographic visualization of the gallbladder.

When there is nonvisualization it is rather common to see the outline of a fibrotic gallbladder in the roentgenogram. This is probably due to repeated attacks of partial or intermittent obstruction. The changes in the biliary tract also vary with the extent of the infection which tends to persist with gallstones as with kidney stones. There may be no permanent loss of function after temporary obstruction in the ducts, and such gallbladders may be conserved.

From clinical and experimental observations of the frequent presence of precipitated particles of bile or sand, I am convinced that enough attention has not been given to their importance in the production of stasis. Both the cystic duct with its tortuous and valvular outlet, and the terminal portion of the choledochus, with its papilla lined with numerous gland crypts and rosebud folds of mucous membrane, are vulnerable points for obstruction by inflammation from minute particles of bile precipitate.

Obstruction or incarceration from a stone in either of these ducts and infection are frequently seen.

That minute particles of bile precipitate occur rather frequently and may be caught in the valves of the cystic duct or crypts of the papilla is not generally recognized.

Small foreign particles within the cystic or terminal portion of the common duct may lead to spasm, stasis, incarceration, traumatic inflammation and secondary local or extending infection. Primary infections in the bile ducts or extensive lymphangitis may occur without gallstones.

It is known that the liver (E. A. Graham and co-workers [55]) and also the lymph glands of the biliary tract (Judd) may contain pathogenic bacteria, although in the absence of stasis or acute inflammation it is rather unusual to find them in the bile.

An edematous inflamed gallbladder is not due to venous obstruction (Kreider [56]), and I have never found it after experimental ligation of both the cystic artery and the vein, but it resembles acute lymphangitis which extends into the liver.

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55. Graham, E. A.: Hepatitis, Surg., Gynec. & Obst. **26**:521 (May) 1918. Graham, E. A.; Peterman, M. G., and Priest, W. S.: Association of Hepatitis with Experimental Cholecystitis and Its Bearing on Pathogenesis of Cholecystitis in the Human, Arch. Surg. **2**:92 (Jan.) 1921.

56. Kreider, P. G.: Anatomy of Veins of Gallbladder: Their Relation to Impacted Stone, Surg., Gynec. & Obst. **57**:475 (Oct.) 1933.

I believe that the removal of the gallbladder, necessitating the opening of acutely inflamed lymph channels and glands, which Judd and others have found frequently to contain streptococci, or when the bile contains bacteria, may lead to a fatal lymphangitis, peritonitis or hepatitis and cholemia.

If one can diagnose mechanical obstruction of the cystic duct, early operation is decidedly preferable before the development of acute lymphangitis, empyema, cholangeitis or hepatitis with dehydration and toxemia.

If operation is not performed early, one should limit the procedure, if possible, to simple drainage of the gallbladder or ducts. In the presence of infection in the biliary tract or liver, two stage operations may be necessary to remove the gallbladder or stones from the common duct and occasionally from the cystic duct. Smears of the bile for bacteria should be made more freequently at operation. In the presence of bacteria, especially streptococci, one should usually limit the operation to drainage.

Under certain critical conditions the removal of only the mucosa may be indicated (W. J. Mayo [57]). Partial excision of the gallbladder (as practiced by Estes [58]) or partial excision and destruction of the unexcised mucosa of the wall of the gallbladder adherent to the liver with cautery (Rutherford Morison) or by electrocoagulation (Thorek [59]) should be of definite value in limiting infection. These procedures avoid opening the large anastomosing vascular, lymph and biliary channels and prevent the extension of the infection into the liver.

In the absence of biliary stasis or infection there are disadvantages in drainage of the gallbladder which seriously impairs function, although there is a low mortality, and in cholecystectomy, which produces changes in the common duct and liver.

CLINICAL STUDIES

A study of the physiology, operative results and experimental findings indicates that immediate suture of the gallbladder may be desirable under the following conditions: (1) after negative exploration of the gallbladder; (2) after removal of gallstones, especially a solitary one with good function of the gallbladder; (3) in a patient who is old or is a bad risk, after removal of stones in a functionless gallbladder but without inflammation or stasis in the biliary tract; (4) after cholecystotomy, when the common duct is opened and drained in the absence

57. Mayo, W. J.: Cholecystectomy, J. A. M. A. **35**:1396 (Dec. 1) 1900.

58. Estes, W. L.: Partial Cholecystectomy, Arch. Surg. **23**:119 (July) 1931.

59. Thorek, M.: Electrosurgical Obliteration of the Gallbladder, J. A. M. A. **103**:169 (July 21) 1934.

of acute inflammation, and (5) after excision of a solitary benign tumor in the wall of a functioning gallbladder.

The following cases in which cholecystotomy with primary suture was done illustrate when this procedure may be indicated and demonstrate that function of the gallbladder may be preserved.

CASE 1.—*Solitary large gallstone impacted in the neck of the gallbladder with hydrops and chronic cholecystitis, angina pectoris and diabetes mellitus.*

B. A., a moderately obese man aged 49, had frequent attacks of angina and chronic myocardial damage. Subtotal thyroidectomy was performed two years previously for hyperthyroidism, although the patient was a bad surgical risk. Severe attacks referable to the gallbladder occurred over ten years, with almost constant pain and distress the last fifteen months, which was aggravated on eating. The patient had been under treatment for several years for marked diabetes. The blood pressure was 200 systolic and 120 diastolic. On March 29, 1933, and on April 14, 1934, roentgen examinations failed to visualize the gallbladder.

On May 2 operation revealed hydrops of the gallbladder with a wall 4 cm. thick due to complete obstruction of the neck by a solitary incarcerated cholesterol stone, measuring 2 by 2.5 cm. in diameter. The liver was moderately enlarged, and the surface was thickened. There was a palpable lymph gland along the cystic duct. An incision was made in the fundus, and the incarcerated gallstone was milked up and removed. The cystic duct was found to be patent, and the incision was closed with two rows of fine catgut. The wound was closed without drainage. On June 22, seven weeks after operation, roentgen examination failed to visualize the gallbladder. On Dec. 22, 1934, Feb. 8, 1935, and Feb. 18, 1936, there was good visualization of the gallbladder with emptying one hour after a fatty meal, and there was a normal duodenal bulb after a meal of barium sulfate. On February 23 there was complete relief from the symptoms referable to the gallbladder but a persistence of the attacks of angina. The patient was active but considerably overweight.

CASE 2.—*Solitary large stone with chronic cholecystitis and attacks of intermittent obstruction.*

J. D., a poorly nourished man aged 68, had attacks of gallbladder colic for the past eight years which became more frequent and finally occurred once or twice a week, with pain and tenderness over the upper portion of the abdomen. On June 24, 1935, roentgen examination failed to visualize the gallbladder. The Wassermann reaction was negative, and the icterus index, 5.

On July 8 operation revealed a moderately enlarged and thickened gallbladder with one gallstone, measuring 3.2 by 1.7 by 1.4 cm. in diameter. No stones or pathologic process was found in the ducts. The cystic duct was patent. There was moderate chronic hepatitis. An incision was made in the fundus of the gallbladder, the stone was removed and the edges of the wound were sutured with fine catgut sutures. The abdominal wound was closed without drainage. Mild pneumonia developed postoperatively in the lower lobe of the right lung, which was demonstrated roentgenographically. Microscopic examination of the gallbladder showed a normal wall, except for an increase in small round cells around the blood vessels of the subserous tissue. The patient was discharged from the hospital on August 1, with no complaints. On September 18 roentgen examination failed to visualize the gallbladder. On October 1 examination gave negative results, and the patient was relieved of his symptoms.

CASE 3.—*Solitary stone in the gallbladder. Acute attacks of auricular fibrillation and tachycardia with coronary and myocardial damage.*

M. S., a slightly obese woman aged 56, had severe attacks of auricular fibrillation and tachycardia with occasional collapse for a few months preceding operation. She suffered from abdominal distress with gas and belching at times but no colic. An electrocardiogram taken during an attack showed auricular fibrillation with tachycardia and mild myocardial and coronary damage. Complete roentgen studies of the gastro-intestinal tract, the kidneys and the chest gave negative results as did the laboratory examinations. The blood was normal. The roentgenogram showed good visualization and normal function of the gallbladder, which contained one large gallstone.

Operation on Oct. 7, 1935, showed a slightly enlarged gallbladder which contained one large cholesterol stone. There was slight chronic hepatitis. An incision was made in the fundus of the gallbladder, which appeared normal grossly, and the stone was removed. The incision was sutured carefully with fine catgut, and a piece of omentum was sutured over it. A small drain was left in the abdomen for twenty-four hours. Recovery was uneventful, and the patient was discharged from the hospital on the twelfth day. On Jan. 15, 1936, she had one mild cardiac attack. On February 18 roentgen examination showed good visualization and function of the gallbladder. On May 27 there were no further cardiac attacks or complaints.

CASE 4.—*Small adenoma of the fundus of the gallbladder. Chronic duodenal ulcer with high grade retention.*

W. C., a well developed man aged 49, who was moderately emaciated, presented a typical history of ulcer with periods of distress from two to three hours after meals for five years. There was a loss of 55 pounds (24.9 Kg.) of weight and constant distress after eating in the year preceding operation. Some relief was obtained by the ingestion of milk or mucin. Frequent attacks of vomiting occurred a few months before operation. During two weeks' treatment for ulcer in the hospital 1,000 cc. of the contents of the stomach was aspirated each night. There was no history of colic or pain referable to the gallbladder. The stools showed blood constantly.

Operation on July 14, 1934, revealed a characteristic chronic duodenal ulcer with a high grade stenosis and a few adhesions to the side of the gallbladder. A posterior gastrojejunostomy was performed. There was a small nodule in the fundus of the gallbladder 1 cm. in diameter. This nodule was excised, including the entire thickness of the wall of the gallbladder. The mucosa was inspected through the incision, but no other changes were seen. The incision was sutured with fine catgut and covered with omentum. The abdominal wound was closed without drainage. Convalescence was uneventful. The microscopic diagnosis was benign adenoma of the gallbladder. The patient was discharged from the hospital on Aug. 1, 1934. On August 25 a roentgenogram showed some visualization of the gallbladder. On September 17 the patient had no complaints. There was a gain of 30 pounds (13.6 Kg.) in weight after the operation.

Comment.—Cholecystotomy with primary suture of the gallbladder was performed on three of the four patients for removal of solitary stones and on the fourth for an adenoma of the fundus, which was excised. All of the patients were poor risks; two had symptoms of severe cardiac damage, the third was 68 years old and poorly nourished

and the fourth was emaciated and had a high grade stenosis due to a duodenal ulcer. In all but the third case, in which a drain was removed on the second day, the abdominal wounds were closed without drainage. None of the patients have had any evidence of recurrence of gallstones. In three of the four cases the function of the gallbladder was demonstrated after operation by roentgenographic visualization.

In the first case, in which the gallbladder was thickened and the cystic duct obstructed, there was no visualization seven weeks after operation, but at six months and one and one-half years there was good function. In the second case, in which a thickened chronically inflamed gallbladder was found at operation, there was no visualization after five weeks, and no further tests have been made. In the third case, in which function was normal before operation, there was good visualization when the patient was tested after four months. In the fourth case there was some visualization after five weeks.

It is shown here that with a normal or even a considerably thickened gallbladder due to intermittent or complete obstruction function may return in from five to ten weeks after cholecystotomy with primary suture.

DISORDERS OF THE COMMON DUCT

Recent statistics point to an increasing frequency of stones developing in the common duct after removal of the gallbladder or after loss of function (Judd,[60] Beye[61] and Hunt[62]).

Evidence is given by Rufanov[63] of the occasional development of stones in the substance of the liver or the intrahepatic bile ducts (Rovsing[64]). This indicates that measures other than removal of the gallbladder, such as the correction of diet, removal of foci of infection and proper exercises, are necessary in the presence of a diathesis to gallstone formation.

The common duct as a rule is found dilated after removal of the gallbladder (Judd and Mann), although there may be a temporarily incompetent sphincter.

If the sphincter remains incompetent, Rost[65] has observed that there is no compensatory dilatation of the common duct.

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60. Judd, E. S.: Disease of the Biliary Tract, S. Clin. North America **15**:1073 (Oct.) 1935.

61. Beye, H. L.: Conditions Necessitating Surgery Following Cholecystectomy, Tr. West. S. A. **44**:450, 1934.

62. Hunt, V. C.: Liver in Relation to Surgical Treatment of Lesions of Extrahepatic Bile Ducts, California & West. Med. **43**:278 (Oct.) 1935.

63. Rufanov, Ivan G.: Liver Stones, Ann. Surg. **103**:321 (March) 1936.

64. Rovsing, T.: Gallstones Cause, Not the Result of Infection, Acta chir. Scandinav. **56**:207, 1923.

65. Rost, F.: Die funktionelle Bedeutung der Gallenblase, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **26**:710, 1913.

The tone of the sphincter may be partially or completely gone, thereby lessening biliary stasis and the tendency to the formation of stones without necessarily causing the loss of the protecting folds of mucosa in the papilla with regurgitation from the duodenum.

A spastic or stenosed sphincter may predispose to infection or to the formation of stones, especially in the presence of a diathesis. The occurrence of gallstones in the gallbladder is much less serious than in the common duct.

A fibrotic gallbladder may be left under certain conditions, especially if the cystic duct is found to be dilated, and the operation may be limited to the relief of stasis of the common duct.

One should attempt to produce a moderate amount of incompetency of the sphincter of the common duct when biliary stasis is due to spasm, papillitis, ampullitis or cholangeitis, either with or without gallstones.

If stasis is due to acute inflammation of the biliary tract or pancreas, simple biliary drainage will usually permit the swelling to subside.

When considerable resistance is found at the outlet of the common duct, cautious dilatation may be followed in certain instances by the use of an indwelling catheter.

Diminution of the action of the sphincter may be obtained by cutting, by dilatation or by leaving a rubber tube in it.

Cutting the sphincter should be done through a duodenotomy incision and followed by a plastic suture. Unless deep cuts are made in the wall of the duodenum, there will be no permanent dilatation. If severe dilatation or deep cuts are attempted through the common duct, the wall may be perforated, with leakage and peritonitis (Allen [66] and Lahey [67]). Experimentally, I [68] observed that dilatation of the sphincter by a pressure of 250 mm. of mercury produced only a temporary decrease in tone. Severe instrumental dilatation was necessary to produce permanent dilatation, as measured several weeks later. Moderate dilatation resulted in a decrease of the resistance of the sphincter to about one-half normal.

A rubber tube passed through the sphincter and left for some time produced some permanent dilatation, but cultures taken later from the liver were frequently positive, suggesting ascending infection. Normally the sphincter and papilla guard the bile ducts from ascending parasites, foreign bodies and infection. Under certain pathologic or anatomic

66. Allen, A. W.: Diagnosis and Treatment of Stones in the Common Bile Duct, Surg., Gynec. & Obst. **62**:347 (Feb.) 1936.

67. Lahey, F. H.: Stones in the Gallbladder and Bile Ducts, S. Clin. North America **15**:1459 (Dec.) 1935.

68. McWhorter, G. L.: The Surgical Significance of the Common Bile Duct Sphincter, Surg., Gynec. & Obst. **32**:124 (Feb.) 1921.

conditions of the bile passages and possibly also of the pancreas, a diminution of its action may be desirable. In the presence of a high grade congenital or fibrous stenosis anastomosis of the biliary tract to the stomach or duodenum may be necessary. Recent experimental work of Gentile [69] indicates that the danger of ascending infection in the absence of stasis has been overemphasized.

In deciding whether operation is indicated in disease of the biliary tract one must be guided by the gross appearance of the liver, the common duct and the gallbladder.

A small common duct with a thin wall should indicate that the disease was limited to the gallbladder or that there was a primary incompetent sphincter. A dilated common duct with a slightly hypertrophied wall might indicate a competent sphincter with a functionless gallbladder or the absence of the gallbladder. Exploration of the duct would not necessarily be indicated in either condition.

A dilated common duct with a thin wall associated with jaundice but without stones in the gallbladder would suggest high grade or complete obstruction at the outlet of the duct by carcinoma, local inflammation or extramural pressure.

A common duct with a thick muscular wall and some dilatation would suggest incomplete or intermittent obstruction.

A dilated fibrotic common duct associated with jaundice and stones in the gallbladder would suggest an obstruction at the terminal portion of the duct by stones or by a stenosis with infection. Exploration of the common duct and occasionally anastomosis of the gallbladder would be indicated.

Bernhard [70] reported on a thousand choledochotomies, with a mortality of 9.9 per cent, there being three times more men than women in his group of patients. Icterus was the chief indication, this symptom being absent in only 19 per cent. Among the patients followed up after operation, about one-third had some complaints and 11 per cent had severe complaints, usually due to cholangeitis and hepatic damage, while recurrence of stones was rare. Chronic pancreatitis was present at operation in about 10 per cent.

OPERATIONS ON THE COMMON DUCT AND GALLBLADDER

The following cases illustrate six different pathologic conditions of the common duct in which primary suture of the duct, gallbladder or of both was done.

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69. Gentile, A:. Cholecystogastrostomy and Hepatitis: Experimental Study, Arch. Surg. **30**:449 (March) 1935.

70. Bernhard, F.: Ueber die Erfahrungen bei 1000 Choledochotomien aus den Jahren 1895-1932 und ihre Spätergebnisse auf Grund von Nachforschungen bzw. Nachuntersuchungen, Deutsche Ztschr. f. Chir. **246**:1 (Dec. 10) 1935.

CASE 1.—*Gallstones in the gallbladder and common duct. Patent ampulla, but recent obstructive jaundice. Cholecystolithotomy and choledocholithotomy* (fig. 1*A*).

A. S., a man aged 62, after six weeks of complete jaundice underwent an exploratory operation five months before the present operation, and a clinical diag-

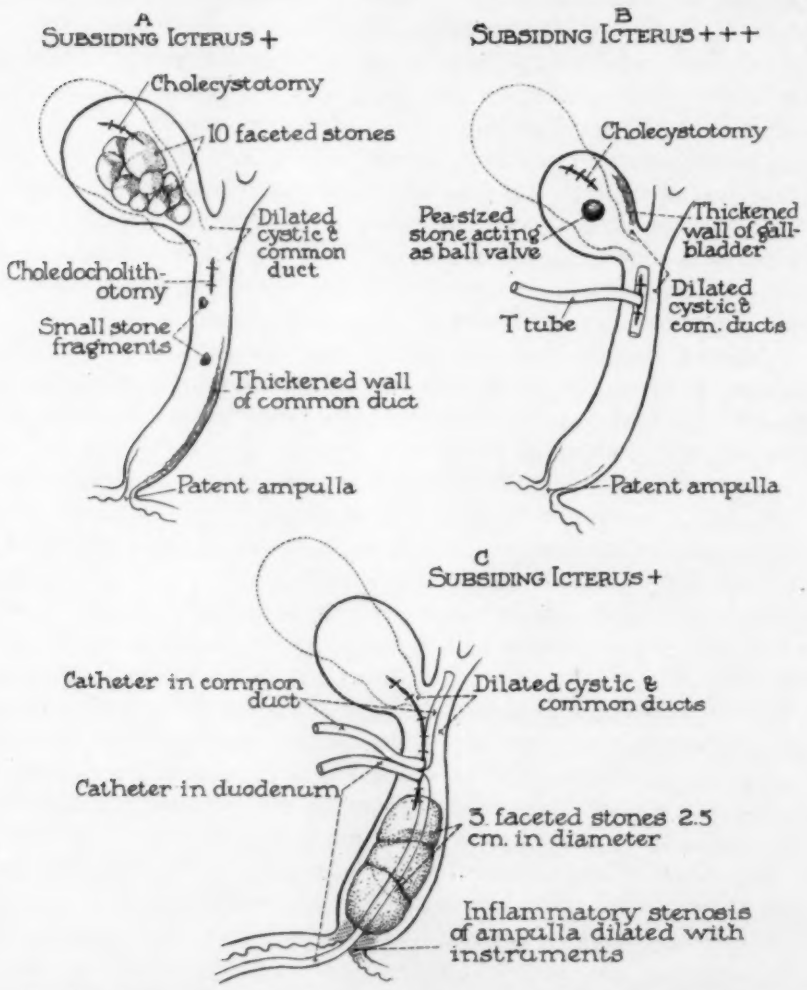

Fig. 1—Diagrammatic drawing showing three pathologic conditions in which different operations were performed on the common duct and the gallbladder with primary suture of duct in one (*A*) and of the gallbladder in all (*A*, *B* and *C*).

nosis of inoperable carcinoma of the pancreas was made; the gallbladder was drained. The present complaints were complete obstructive jaundice of five weeks' duration with acholic stools. Recently the jaundice subsided suddenly to only a trace. On Aug. 16, 1934, roentgen examination failed to visualize the gallbladder, but the thick walls cast a shadow. .

When operation was performed on August 30 there was slight icterus. Ten large faceted stones were removed from the moderately thickened gallbladder, followed by primary suture. Two small crumbs of a stone were removed from a slightly thickened common duct, which was closed by primary suture after the ampulla was found to be patent to a no. 12 French catheter. An incisional hernia was repaired, and an abdominal drain was inserted through a stab incision. Recovery was uneventful. The patient was discharged from the hospital on September 17.

CASE 2.—*Small solitary gallstone in the gallbladder with dilated cystic and common ducts. Patent ampulla but a recent obstructive jaundice and extensive fibrosis of the biliary tracts. Cholecystolithotomy and choledochostomy* (fig. 1*B*).

T. C., a man aged 46, suffered from an extensive myocardial damage with fibrillation and hemiplegia for one year. He had marked obstructive painless jaundice of two months, which was slightly decreasing. On Aug. 21, 1935, the icterus index was 80. The stool contained blood but no bile. On August 24 the icterus index was 54.

At operation on September 6 a "ball valve" stone, 0.7 cm. in diameter, was removed from a small fibrosed gallbladder with a dilated cystic duct 1 cm. in diameter. Primary suture of the gallbladder was done. In order to prevent any later bleeding, a fine catgut suture was tied about the cystic duct and blood vessels. The mucosa of the terminal end of the common duct was thickened and friable, and the ampulla was patent and contained no stones. A T tube was inserted. The jaundice cleared up in three weeks. Four weeks after the operation the T tube was removed. Recovery was uneventful. The patient was discharged on September 30.

CASE 3.—*Large gallstones in the common duct with a slight inflammatory stenosis of the ampulla. Extensive fibrosis of the biliary tract, with dilated cystic and common ducts and a small gallbladder. Cholecystotomy and choledocholithostomy* (fig. 1*C*).

L. K., a man aged 64, had had acute symptoms characteristic of attacks of gallbladder disease for several years, with recent attacks of jaundice, vomiting, clay colored stools and soreness in the right upper quadrant but no pain. There was a recent jaundice of three weeks' duration. On Oct. 30, 1935, the icterus index was 30, and the cholesterol content, 150. On November 7 the gallbladder was faintly visualized. Roentgenograms of the gastro-intestinal tract were normal.

When operation was performed on November 8 there was slight icterus and the gallbladder was found to be small and fibrosed. Three 2 cm. faceted and partially embedded stones were removed from a dilated common duct, and the incision was continued into the dilated cystic duct and gallbladder, which had no stones. The inflammatory stenosis of the ampulla was dilated, and a no. 12 catheter was inserted into the duodenum and brought out through the wound. A second catheter was placed in the hepatic duct. The incision into the gallbladder and cystic duct was sutured tightly. A scar of a duodenal ulcer was present. After a few days the bile formed a precipitate in the drainage tube, making daily irrigation necessary. The tubes were removed after three weeks. Recovery was uneventful. On December 8 the icterus index was 6. The patient was discharged on December 8. At examination on Jan. 10, 1936, no complaints were elicited.

CASE 4.—*Complete stricture of the common duct and obstruction of the cystic duct by a stone with empyema and multiple stones in the gallbladder. Choledochotomy with flap duodenocholedochostomy and cholecystolithectomy* (fig. 2*D*).

P. L., a woman aged 70, had had many previous mild attacks referable to the gallbladder. The blood pressure was 210 systolic and 90 diastolic. There was

complete obstructive jaundice of three weeks' duration with chills and fever but no colic. On Sept. 13, 1935, the icterus index was 88, and on September 17, it was 92. There was blood but no bile in the stools. Roentgen examination, which was done elsewhere, failed to visualize the gallbladder. The condition of the patient became progressively worse.

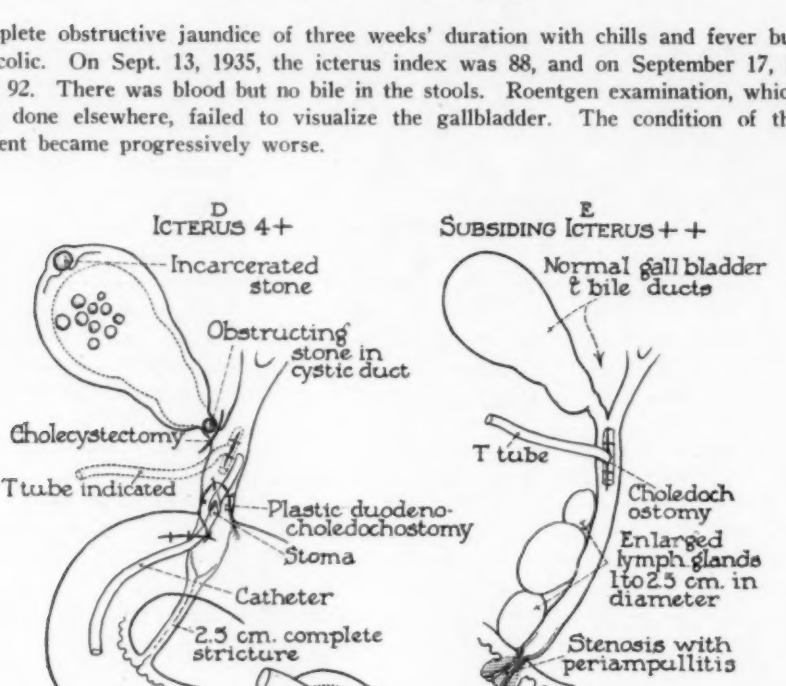

Fig. 2.—Diagrammatic drawing showing operations on the common duct, with dilation of the outlet and without disturbing the gallbladder (*E*) and with plastic correction of a terminal stenosis (*D* and *F*) and combined with removal of the gallbladder (*D*) or with drainage (*F*).

Operation on October 1 showed the liver to be green and the gallbladder enlarged and indurated with mucopurulent contents and stones. One was embedded in the necrotic mucosa of the fundus and one completely obstructed the small cystic duct. The gallbladder and stones were removed. The common duct was enlarged

except the terminal 3 cm., which was indurated, forming an impassable stricture. Choledochoduodenostomy was performed, with a duodenal flap sutured around an opening low in the common duct over a rubber tube. The opening in the common duct was sutured tightly, with drainage of the abdominal wound. The temperature was 103 F. for the first two days postoperatively. The patient improved until the ninth day, although there was a biliary fistula, when cardiac decompensation and death suddenly occurred.

CASE 5.—*Stenosis of the ampulla due to pericholedochitis at the terminal portion and pressure from enlarged lymph glands. Normal gallbladder and common duct with absence of stones. Obstructive subsiding jaundice. Subacute chronic appendicitis. Choledochostomy with T tube; dilatation of sphincter; appendectomy (gallbladder undisturbed)* (fig. 2*E*).

S. F., a Negro aged 35, gave a history of repeated alcoholic bouts. He had had obstructive painless jaundice for five weeks, which was gradually subsiding. On Oct. 2, 1935, the gallbladder was palpable. The icterus index was 105. Drainage with a duodenal tube gave no relief. Roentgen examination of the gastrointestinal tract gave negative results. The jaundice became less marked.

At operation on October 28 the gallbladder and walls of the common duct appeared to be normal. The common duct was opened, but no stones were found. There was slight stenosis of the ampulla, which was dilated, and a T tube drain was inserted. Five large lymph glands were removed from the side of the common duct. A kinked subacutely inflamed appendix was removed. The microscopic report on the glands along the common duct, measuring from 1 to 2 cm., was simple hyperplasia. After the injection of iodized poppy-seed oil 40 per cent through the T tube on November 16 visualization showed the outlet to be patent, and the tube was removed. The icterus index on November 8 was 31, and on November 15 it was 8. Convalescence was uneventful. The patient was discharged on November 27. Observation on Jan. 10, 1936, elicited no complaints. On April 8 slight visualization of the gallbladder was observed. On May 25 the patient was in excellent condition with no complaints, although he frequently became inebriated.

CASE 6.—*Complete inflammatory stricture of the ampulla of the common duct around a gallstone crumb, with "white" bile and subacute cholecystitis. Cholecystostomy, choledochostomy and duodenotomy with ampulloduodenorrhaphy and ampullolithostomy* (fig. 2*F*).

F. C., a woman aged 24, had had painful attacks referable to the gallbladder for one year. The present attack associated with vomiting and jaundice began five weeks before operation, becoming complete ten days before. The icterus index on Aug. 22, 1935, was 63; on August 24 it was 74, and on August 28 it was 96.8. The hemoglobin content was 58 per cent; the red blood cells numbered 4,560,000, and the white blood cells, 11,950. The stools were acholic. A transfusion of blood was given.

At operation on September 9 the liver was found to be congested, and the gallbladder and common duct were enlarged and thickened. They were opened and found to contain white bile, but no stones were seen. There was complete obstruction at the ampulla due to a palpable spherical mass. The duodenum was opened, and the papilla and ampulla were found to be surrounded by an inflammatory mass 2 cm. in diameter. The papilla was split open, and an inflammatory stenosis with a small crumb of a gallstone was found incarcerated in the end of the ampulla. The cut sides of the ampulla were sutured to the duodenum, a short rubber tube

was inserted into the common duct and the duodenum was closed. A tube was also inserted in the common duct and a drainage tube in the gallbladder. The gallbladder drain was removed after three weeks and the T tube after four weeks. There was uneventful convalescence. The patient was discharged on October 9.

Comment.—These six cases with evidence of obstructive jaundice illustrate different problems in operations on the common duct in which an exploratory incision of all or a part of the biliary tract may be followed by primary suture alone or combined with drainage.

All six of the patients, with perhaps one exception (S. F.), were poor risks and suffered from jaundice, which was complete in two cases, with "white" bile in one. Three were over 60 years old, and one had severe cardiac damage. A careful study had been made of each patient before operation, and it was believed that nothing could be gained by further medical treatment.

In the first case, after jaundice for several weeks the gallbladder was drained owing to an incorrect diagnosis of inoperable carcinoma of the head of the pancreas, five months previous to a second operation. The ten faceted stones found at the second operation had undoubtedly formed since the first one, the formation being favored by biliary stasis. Primary suture of both the common duct and the gallbladder with the insertion of a safety drain in the wound was done to conserve function and to shorten the postoperative disability, since the ampulla was patent.

The patient in the second case was a bad risk because of the cardiac condition. There was a recent subsidence of an obstructive icterus. The common duct was patent, the cystic duct was dilated and the gallbladder was fibrosed and contained a small stone covered with fragments of mucous membrane, indicating recent impaction in the common duct. The incision in the gallbladder was sutured, and the common duct was drained with a T tube to relieve the icterus. Temporary occlusion of the cystic duct was done with a catgut ligature to prevent any later bleeding from the sutured incision.

In the third case the gallbladder was small and fibrotic and the common duct thickened and dilated with three large faceted stones in it, producing some necrosis of the mucosa and inflammatory stenosis of the outlet. This was dilated, and a small catheter was passed into the duodenum and another into the hepatic duct.

In the fourth case, in which the symptoms were complete obstructive jaundice, chills and fever, the patient was a poorly nourished woman of 70 years, with hypertension and cardiac damage. There was a complete stricture of the common duct. Anastomosis of the gallbladder to the stomach could not be done because there was an incarcerated stone in the cystic duct and an empyema of the gallbladder. The gallbladder and stones were removed. A flap was cut, and an

anastomosis was made from the duodenum to the common duct. A catheter should have been left in the duct on account of the icterus and to relieve the pressure from the anastomosis. However, a leakage of bile developed along the abdominal drain, with no local reaction. The patient died of cardiac weakness on the ninth day, after an early hyperpyrexia had subsided. Simple drainage of both the common duct and the gallbladder might have given temporary relief, and a second operation could have been performed under better conditions. I [71] have previously reported the case of a patient in whom hepaticoduodenostomy was successful for over thirteen years.

In the fifth case a complete obstructive jaundice was subsiding. There was a normal appearing gallbladder and common duct, with compression by large lymph glands. The glands were removed, and exploration of the common duct showed it to be slightly narrowed at the outlet. It was dilated easily, and a T tube was inserted. The gallbladder, which appeared normal, was not opened. A subacutely inflamed appendix was removed. Either the large hyperplastic lymph glands or a primary papillitis may have obstructed the duct. There was a patent outlet, as shown after choledochography through the T tube, and complete recovery resulted. It is possible that an incompetent sphincter may have been the cause of the nonvisualization of the gallbladder seven months after operation, although the patient was free from symptoms.

In the sixth case there was a persisting complete obstructive jaundice. A thickened dilated gallbladder and common duct were explored, and both contained "white" bile without visible stones. An inflammatory mass in the region of the ampulla was found on incision after duodenotomy to be an inflammatory stenosis of the papilla surrounded by a zone of inflammation. When the papilla was incised a fine crumb of a gallstone not over 1 by 2 mm. in size was found incarcerated in the swollen mucosa. It was removed, and the cut sides of the ampulla were sutured to those of the duodenal mucosa around a small rubber tube. A T tube was placed in the common duct and a drain in the gallbladder. Convalescence was uneventful.

Gas with local anesthesia or local anesthesia alone was used in all of the clinical cases reported.

In the postoperative treatment of most patients after biliary operations one must guard against dilatation of the stomach, but continuous aspiration of the gastric contents with a catheter predisposes to bronchitis and pneumonia.

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71. McWhorter, G. L.: Congenital Cystic Dilatation of the Common Bile Duct, Arch. Surg. **8**:604 (March) 1924; Results of Reconstruction of Common Bile Duct, S. Clin. North America **12**:159 (Feb.) 1932.

The differential diagnosis of inflammatory stenosis of the ampulla, with or without stones, from a malignant growth of the ampulla, common duct or pancreas and chronic pancreatitis is difficult, particularly when there is blood in the stools and no pain. Inflammatory changes in the terminal portion of the common duct, with or without stones, should be considered more frequently as the cause of obstructive jaundice.

CONCLUSIONS

1. The frequency of gallstone particles or crumbs has been observed experimentally and clinically. It is probable that their clinical occurrence has been overlooked in causing transient colic or spasm and, when incarcerated in the ampulla or papilla, in the production of edema, stasis and infection of the ducts, liver, gallbladder and pancreas.

2. The biliary tract and liver easily react to chemical changes and trauma by inflammation, after which there may be precipitation of bile. Caution should be observed in the use of the dye or opaque mediums injected intravenously in the presence of inflammation or obstruction in the biliary tract.

3. Temporary ligation of the bile ducts with fine catgut may aid in controlling hemorrhage, especially about the cystic duct, and in the diversion of bile.

4. Experimentally, after splitting the gallbladder and occluding the cystic duct, healing occurs rapidly, usually with a tendency to fibrosis. In the absence of stones or infection there is no unusual change in the liver. Clinically, on the other hand, with obstruction and stones of the cystic duct, extensive inflammation of the gallbladder and liver, which may be due to infection, frequently occurs.

5. Conservation of the gallbladder in the presence of any function may prevent later changes in the common duct leading to stasis and the formation of stone. When indicated, exploratory opening and even wide splitting of the gallbladder may be done and may be followed by primary suture. The gallbladder may be left unopened when the disturbance is found to be limited to the common duct.

6. Primary suture of the gallbladder may more nearly restore physiologic function and avoid complications than either drainage or removal in selected cases. Drainage of either the gallbladder or the common duct is desirable in acute inflammation and stasis, but with extensive chronic disease cholecystectomy is usually indicated.

7. Leaving alone a functionless gallbladder, especially one with a dilated cystic duct, may be preferable, especially in a patient who is a poor risk, and probably will not increase the formation of stones in the common duct. Conservation of the gallbladder, when feasible,

will definitely lower the immediate mortality and make an operation for stones in the common duct or for stenosis safer. In the presence of biliary stasis or diathesis, gallstones may reform in either a functioning or a nonfunctioning gallbladder or in the common duct.

8. There is an increasing frequency of pathologic conditions of the common duct. This is due not only to the clinical frequency of systemic changes leading to disease of the biliary tract and primary disturbances in the terminal portion of the choledochus but to further changes in the common duct resulting from unnecessary drainage or removal of still functioning gallbladders.

9. Papillitis or ampullitis may exist with local inflammation and lymphadenopathy but with an otherwise normal biliary tract. This may arise from spasm and irritation of minute crumbs of gallstones and from extension of infection from the duodenum or other foci, such as appendicitis.

10. A better understanding of disturbances of the biliary tract and their pathologic changes should lead to earlier operation with more frequent correction of disorders of the common duct and to greater conservation of the gallbladder with better end-results and a lower mortality.

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THROMBO-ANGIITIS OBLITERANS AND TYPHUS

EVIDENCE OF ETIOLOGIC RELATIONSHIP

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The history of medicine makes it axiomatic that diseases of unknown etiology have given rise to innumerable measures for their relief. Success in therapy, however, with few exceptions, was attained only on the discovery of the causative factor. In this respect thrombo-angiitis obliterans is typical. The literature of the last three decades reveals hundreds of therapeutic suggestions which have been tried and which have yielded little success. This may be attributed to the fact that of all the peculiar etiologic agents which have been suggested, none up to the present time has proved to be the real cause of the condition. Among the causes which have been advanced may be mentioned ethnologic predisposition, metabolic disturbances, climatic and balneologic conditions, endocrine disturbances and syphilis. The toxic effects of drugs and chemicals, such as tobacco, alcohol and ergot, have also been suggested as the possible cause of the disease. However, none of these has as yet been proved.

ETIOLOGY

Race.—It has been generally believed that thrombo-angiitis obliterans is peculiar to the Jewish race, largely because a number of years ago the majority of cases observed in this country occurred among poor Jewish immigrants from Russia and Poland. As a matter of fact, this people has been so scattered and intermarried that a pure Jewish strain can scarcely be said to exist. In discussing this subject, Friedman [1] in 1920 stated that he had seen the disease in Estonians and Russians as well as in Jews. It has been noted chiefly among Jews because few Estonians and Russians have migrated to this country. At this time Frauenthal [2] said that he had seen over 900 cases of

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1. Friedman, G. A., in discussion on Buerger, Leo: The Pathology of Thrombo-Angiitis Obliterans, M. Rec. **97**:457-458 (March 13) 1920.

2. Frauenthal, in discussion on Buerger, Leo: The Pathology of Thrombo-Angiitis Obliterans, M. Rec. **97**:457-458 (March 13) 1920.

thrombo-angiitis obliterans and that 90 per cent of them were in Russian, Polish and Austrian Galicians; he believed, therefore, that the presence of the disease depended on location. Kukin [3] reported 70 cases in Russians, only 3 of whom were Jews. Schum [4] stated that in Russia the disease was just as common among gentiles as among Jews. Meleney and Miller [5] reported a series of 25 cases of thrombo-angiitis obliterans which occurred in China. Ludlow [6] saw over 100 cases in Korea, and Koga [7] spoke of the disease being common in Japan in 1913. Telford and Stopford [8] in 1924 reported 4 cases in non-Jewish British subjects. Weber, Rast and Lutterotti [9] also described 3 cases in Englishmen without Jewish ancestry and stated that they had seen other cases in the London hospital in persons apparently without Jewish ancestry. Huguenin, Albot and Moldovan [10] cited 3 cases in Frenchmen who were non-Jews, and Orr [11] reported 6 cases in American-born persons without Jewish ancestry. In discussing the etiology of thrombo-angiitis obliterans, Scupham [12] wrote that race should no longer be considered an important factor and reported in detail a case of the typical disease in a Negro. Ochsner stated that he encountered thrombo-angiitis obliterans among Scandinavians in Chicago, while Matas and others reported having seen it in native Americans in New Orleans and elsewhere.

Tobacco.—The prevailing opinion that tobacco enters largely into the causation of the disease does not appear to have a rational basis. Although many persons with thrombo-angiitis obliterans give a history of excessive smoking, in view of the greater use of tobacco an increasing

3. Kukin, N. M.: Obliterating Endarteritis in Women, Sovet. khir. (no. 1) **6**:40-43, 1934.

4. Schum, H.: Das Krankheitsbild der juvenilen Gangrän, Beitr. z. klin. Chir. **146**:551-591, 1929.

5. Meleney, F. L., and Miller, G. G.: A Contribution to the Study of Thrombo-Angiitis Obliterans, Ann. Surg. **81**:976-993 (May) 1925.

6. Ludlow, A. I.: Thrombo-Angiitis Obliterans: A Review and Report of the Disease in Koreans, China M. J. **45**:487-514 (June) 1931.

7. Koga, G.: Zur Therapie der Spontangangrän an den Extremitäten, Deutsche Ztschr. f. Chir. **121**:371-382, 1913.

8. Telford, E. D., and Stopford, J. S. B.: Thrombo-Angiitis Obliterans, Brit. M. J. **2**:1035-1037 (Dec. 6) 1924.

9. Weber, F. P.; Rast, H., and Lutterotti, O.: Thrombo-Angiitis Obliterans in Non-Hebrew Subjects, Brit. M. J. **2**:279-280 (Aug. 23) 1930.

10. Huguenin, R.; Albot, R., and Moldovan, S.: A propos de deux cas de thrombo-angéite oblitérante chez des sujets non-israélites, Ann. d'anat. path. **8**: 176-183 (Feb.) 1931.

11. Orr, T. G.: Thrombo-Angiitis Obliterans a Universal Disease, J. Missouri M. A. **22**:174-175 (May) 1925.

12. Scupham, G. W.: The Diagnosis of Peripheral Vascular Diseases, Illinois M. J. **70**:516-521 (Dec.) 1936.

incidence of the disease should be expected. Furthermore, since cigaret smoking has become a common custom, it would seem reasonable to expect to find more women afflicted with the disease. It is also worthy of note that in Russia and southeastern Europe, where thrombo-angiitis obliterans is of frequent occurrence, tobacco is a luxury beyond the means of the poor peasants. Harkavy [13] used tobacco pollen, tobacco and other allergens to test for hypersensitivity of the skin in over 200 smokers. The results did not indicate that smokers were more often sensitive to tobacco than to other allergens. Trasoff, Blumstein and Marks,[14] of Mount Sinai Hospital, Philadelphia, made similar tests with tobacco. They stated that their studies did not justify the contention that hypersensitiveness of the vascular system to tobacco is the mechanism of thrombo-angiitis obliterans and coronary disease. They stated that there was no essential difference in the reactivity of the skin of normal smokers and of nonsmokers to tobacco. Friedlander, Silbert and Laskey [15] administered daily intraperitoneal injections of extract of tobacco in Ringer's solution to rats. Of 48 male rats receiving these injections, gangrene of the toes developed in 33 in from five to twelve weeks. In none of 12 female rats treated for from five to six weeks did this lesion develop. In 10 control male rats living under identical conditions, no gangrene developed. The histologic changes in the vessels were not mentioned.

Alcohol.—As for alcohol, it has been found that in persons with arterial disease thought to result from chronic alcoholism the condition is not thrombo-angiitis obliterans.

Ergot.—There are on record [16] a few instances of a person's suffering from ergot poisoning due to overconsumption of diseased rye, but there has been no report of a case of thrombo-angiitis obliterans in such a person. Surely this cause could not be operative in China, where the staple diet is millet and rice, or in Japan, where the population subsists on fish and rice; moreover, a study of the histories of patients with thrombo-angiitis obliterans affords no evidence that ergot

13. Harkavy, J.: Skin Sensitiveness to Extracts of Tobacco Leaf, Tobacco Pollen, Tobacco Seed and to Other Allergens in Two Hundred Normal Smokers, J. Allergy **6**:56-61 (Nov.) 1934.

14. Trasoff, A.; Blumstein, G., and Marks, M.: Immunologic Aspect of Tobacco in Thrombangiitis Obliterans and Coronary Artery Heart Disease, J. Allergy **7**:250-253 (March) 1936.

15. Friedlander, M.; Silbert, S., and Laskey, N.: Toe Lesions Following Tobacco Injections in Rats, Proc. Soc. Exper. Biol. & Med. **34**:156-157 (March) 1936.

16. Kaunitz, J.: Chronic Endemic Ergotism, Arch. Surg. **25**:1135-1151 (Dec.) 1932.

might be a causative factor. McGrath [17] and others have attempted to produce the disease by injection of ergotamine tartrate, but they do not claim that the lesions which developed were definitely those of thrombo-angiitis.

Syphilis.—The view that syphilis might be an etiologic factor can be excluded, as Buerger and Kaliski found the Wassermann reactions of patients with thrombo-angiitis to be almost uniformly negative.

Metabolic Diseases.—Metabolic tests on persons with thrombo-angiitis obliterans made under my supervision at the Beth Israel Hospital gave results in no wise different from those obtained with the tests on normal subjects used as controls.

Climatic Conditions.—The fact that thrombo-angiitis obliterans occurs in almost all climates and latitudes makes a discussion of this question superfluous.

Infectious Origin.—The infectious origin of thrombo-angiitis obliterans was first suggested by Saltikow and later by Buerger,[18] who based his conviction on the following evidence: 1. An acute inflammatory lesion and occlusive thrombosis of the arteries and veins are characteristic lesions. 2. Mechanically and symptomatologically, the thrombotic occlusion is the most important phenomenon. 3. The thrombosis is probably preceded and certainly accompanied by an acute inflammatory stage. 4. The lesion involves deep veins in about 40 per cent and superficial veins of the upper and lower extremities in 20 per cent of the cases. 5. Recent investigations of the veins show that acute lesions in the superficial and in the deep vessels are identical. 6. Histologic changes in the veins point to the existence of an infective process.

Meleney and Miller, who observed 25 cases in Chinese subjects, stated that the source of the disease was of infectious origin. They added that careful search on the part of a number of investigators had failed to reveal any specific micro-organism, though when the disease was once established its victims fell easy prey to secondary infection. MacCallum stated that "there is no doubt whatever that this is a process in which injury to the arterial and venous walls is probably caused by some infectious agent." Allen and Lauderdale,[19] of the Mayo Clinic, stated that most students of thrombo-angiitis obliterans have been impressed by the probability that bacteria or their toxins are important

17. McGrath, E. J.: Experimental Peripheral Gangrene, J. A. M. A. **105**: 854-856 (Sept. 14) 1935.

18. Buerger, L.: Is Thrombo-Angiitis Obliterans an Infectious Disease? Surg., Gynec. & Obst. **19**:582-588 (Nov.) 1914.

19. Allen, E. V., and Lauderdale, T. L.: Accidental Transmission of Thrombo-Angiitis Obliterans from Man to Man, Proc. Staff Meet., Mayo Clin. **11**:641-644 (Oct. 7) 1936.

etiologic factors in the genesis of the disease. They reported a case in which thrombo-angiitis obliterans was transferred from one human being to another. While amputating the toes of a man for thrombo-angiitis obliterans, a Scotch surgeon 45 years of age accidentally pierced the palmar surface of his hand and a finger with a spicule of bone from the patient's toe. A month later, changes in color, pallor and cyanosis were noted in the injured finger. Similar changes soon involved other fingers and left no doubt as to the accuracy of the diagnosis.

Many attempts have been made to reproduce the disease with infective agents. Saltikow inoculated animals with staphylococci, streptococci and tubercle bacilli, but the results were disappointing. Buerger in 1929 produced lesions similar to those of thrombo-angiitis obliterans by transplanting segments of veins affected with phlebitis migrans into human beings. Rabinowitz,[20] of Brooklyn, believed that he had found a certain gram-positive organism with which he could reproduce the disease, but his work was not convincing and received no support. Schmidt-Weyland,[21] of Königsberg, found that intravenous injections of highly virulent streptococci, tubercle bacilli of both human and bovine type and killed colon bacilli produced gangrene in rabbits' ears in 21 of 67 experiments, provided 0.5 cc. of a 1:1,000 solution of epinephrine hydrochloride was injected daily near the base of the rabbits' ears. Horton and Dorsey,[22] of the Mayo Clinic, have tried to reproduce thrombo-angiitis obliterans by implanting streptococci in the teeth of dogs. Likewise, numerous attempts have been made to culture the tissue of amputated limbs, but these have resulted in failure. These failures suggest either an inappropriate host or more likely failure to deal with the etiologic agent.

In a paper read before the New York County Medical Society on March 27, 1916, I [23] stated that for a number of years I had been much impressed with the remarkable latency of bacteria remaining in the body after infectious disease and the development of local foci set up by such bacteria long after the original infection had occurred. At that time I recalled that during a visit to Breslau in 1913 I was informed by two assistants of Professor Kuettner that they had found

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20. Rabinowitz, H. M.: Experiments on the Infectious Origin of Thrombo-Angiitis Obliterans and the Isolation of a Specific Organism from the Blood Stream, Surg., Gynec. & Obst. **37**:353-360 (Sept.) 1923.

21. Schmidt-Weyland, P.: Experimentelle Untersuchungen zur Erzeugung von Gangrän und ihre Beziehungen zur Thrombangiitis obliterans, Klin. Wchnschr. **11**:2148-2151 (Dec. 24) 1932.

22. Horton, B. T., and Dorsey, A. H. E.: Experimental Thrombo-Angiitis Obliterans: Bacteriologic and Pathologic Studies, Arch. Path. **13**:910-925 (June) 1932.

23. Goodman, C., and Bernstein, E. P.: Presenile Gangrene, Thromboangiitis Obliterans, New York M. J. **103**:1073-1074 (June 3) 1916.

gangrene of the extremities to be frequent while they were doing medical service in the Bulgarian campaign. It occurred to me that in view of the great frequency of typhus and cholera in the Bulgarian camps there might be a causal relationship between these infections and the frequent occurrence of gangrene. In a conversation with Dr. Zinsser he informed me that during his visit to Serbia he had observed a considerable number of cases of gangrene of the extremities. Gangrene [24] is mentioned in a number of textbooks as a direct complication of typhus. It practically never occurs as a complication of cholera. A study of the epidemiology of typhus indicates that with the disease there is a coexistent high incidence of thrombo-angiitis obliterans. Starting with these facts, I developed my thesis, proposed in 1916, that typhus bears a definite etiologic relationship to thrombo-angiitis obliterans. In support of this thesis I am now prepared to submit the following data. I wish to expand the evidence for this relationship on epidemiologic, pathologic and experimental lines. It will be necessary first to describe both typhus and thrombo-angiitis obliterans.

TYPHUS

For centuries typhus has been coincident with the filth and squalor engendered of poverty and ignorance, as Hirsch's [25] oft repeated statement gives evidence: "The history of typhus is written in those dark pages of the World's story which tell of the grievous visitations of mankind by war, famine and misery of every kind."

Typhus has been described under various appellations: *tabardillo* in Mexico and *fièvre boutonneuse* in the French colonies of North Africa. Analogous diseases are Rocky Mountain spotted fever and Brill's disease, which are constantly present in the United States, and Japanese River fever and Manchurian fever. The vectors of endemic typhus are the rat flea and the rat louse, in contrast to epidemic typhus, in which the vector is the body louse.

A person who is undernourished, mentally fatigued or subjected to a great deal of privation and misery becomes the victim of infection more readily than one who is in better physical condition. The same applies to animals. Inoculate a rat the physical condition of which has not been reduced to a low state and it is not likely to yield as large a number of rickettsias as one that has been subjected to the devitalizing conditions.

24. Goodman, C.: Presenile Gangrene; Thromboangiitis Obliterans; Further Confirmation of Its Relation to Typhus Fever, M. Rec. **92**:275-276 (Aug. 18) 1917.

25. Hirsch, A.: Handbook of Geographical and Historical Pathology, translated by C. Creighton, London, New Sydenham Society, 1883.

Epidemic typhus was first recognized as a disease entity by Fracastorius [26] early in the sixteenth century, and Tobias Cober noted the relation of typhus to pediculosis in 1606. The disease has a widespread distribution, not only in tropical countries but in temperate and northern regions where the poor herd together in winter and where the body louse thrives and is spread.

The cause of typhus was unknown until 1911, when Ricketts succeeded in isolating the specific organism, known as Rickettsia Prowazeki. Ricketts demonstrated this organism in the blood of patients with typhus, while Prowazek in 1913 found it within the cells of the intestinal lining of typhus infected body lice. It can be transmitted to rats and guinea-pigs.

In 1931 Zinsser reported that he was able to produce an almost pure culture of Rickettsia by scraping the bodies from the tunica vaginalis of guinea-pigs which had been inoculated with the blood of patients with typhus. In 1934 Nigg [27] succeeded in growing Rickettsia, with living tissue as a medium, thereby proving beyond all doubt that rickettsia bodies are real organisms capable of cultivation. A vaccine of killed rickettsias, prepared by Zinsser and Ruiz Castaneda,[28] has produced protective immunity against both the European and the Mexican type of typhus.

Pathologic Picture.—Typhus is primarily a disease of the blood stream with rickettsias eventually embedded in the endothelial cells of the blood vessels. A number of investigators in foreign countries, including Wolff,[29] Wiener,[30] Fraenkel,[31] Jochmann [32] and others, as well as Wolbach [33] in this country, have stressed the fact that the infection often has a predilection for the intimal lining of the vessels of the extremities. Wiener, from postmortem examinations, concluded

26. Fracastorius, H.: De contagione, et contagiosis morbis, Venetiis, apud Juntas, 1574.

27. Nigg, Clara: On the Preservation of Typhus Fever Rickettsia in Cultures, J. Exper. Med. **61**:17-26 (Jan.) 1935.

28. Zinsser, H., and Ruiz Castaneda, M.: Studies on Typhus Fever: XII. The Passive Immunization of Guinea Pigs, Infected with European Virus, with Serum of a Horse Treated with Killed Rickettsia of the Mexican Type, J. Exper. Med. **59**:471-478 (April) 1934.

29. Wolff, B.: Klinische und pathologisch-anatomische Beobachtungen beim Fleckfieber, Beitr. z. Klin. d. Infektionskr. **5**:1-74, 1916.

30. Wiener, E.: Ueber Flecktyphus, Wien. klin. Wchnschr. **29**:117-119 (Jan. 27) 1916.

31. Fraenkel, E.: Zur Fleckfieberdiagnose, München. med. Wchnschr. **62**: 805-808 (June 15) 1915.

32. Jochmann, G.: Lehrbuch der Infektionskrankheiten, Berlin, Julius Springer, 1914, p. 757.

33. Wolbach, S. B.; Todd, J. L., and Palfrey, E. M.: Etiology and Pathology of Typhus, Cambridge, Harvard University Press, 1922.

that the most characteristic pathologic evidence of typhus is the extreme fragility of the walls of the vessels. This may entail thrombotic formation in the vessels of the lower extremities and of other parts of the body.

Fraenkel stated that the vascular lesions consist of cellular infiltration in the neighborhood of the arterioles. The outstanding study of the pathologic picture of typhus is that of Wolbach, who performed thirty-eight autopsies in unquestioned cases of typhus a few hours after death. He found a distinctive pathologic condition of the blood vessels, particularly those of the skin and the central nervous system. He wrote: "This lesion began as a proliferative reaction of the endothelium, followed by a thrombosis that may cause complete occlusion of the vessel."

Symptoms and Diagnosis.—Outspoken typhus is generally recognized by the principal symptoms, which are fever, extreme prostration and the lesions of the skin. An important factor from the standpoint of this thesis is that endemic forms and mild types of the disease occurring in epidemics are often overlooked. Nemschilov [34] stated that the disease is often devoid of symptoms or portrays only indefinite clinical signs, a fact that may be responsible for contagion and propagation. Brill and Baehr [35] wrote that mild abortive forms may occur in persons who have been exposed inordinately to infections and in whom there seems to be some degree of natural immunity. Clinically, it is difficult to diagnose the disease in the abortive form, and many times it is overlooked.

During an epidemic in Boston, Shattuck [36] wrote: "There are cases of socalled typhus fever without eruption in which the symptoms are mild and atypical."

Children particularly escape the severe forms of the disease during an epidemic, so that in later life a negative history of typhus does not indicate that a person has not been mildly infected.

In the diagnosis of typhus, the Weil-Felix agglutinative reaction with Proteus X19 is of value.

Isabolinski [37] and others, of the Statts Institute in Smolensk, U. S. S. R., found the Weil-Felix reaction to be strongly positive in 1 per cent of normal persons. They stated that the test was strongly cor-

34. Nemschilov, S. F.: Ueber Hautreaktion mit Exanthin, Klin. Wchnschr. **13**:59-61 (Jan. 13) 1934.

35. Brill, N. E., and Baehr, G.: Typhus Fever, in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1927, vol. 1, chap. 10, pp. 190-201.

36. Shattuck, G. C.: Typhus Fever in Boston and a Review of the Newer Methods of Diagnosing Typhus, Am. J. Trop. Med. **2**:225-250 (May) 1922.

37. Isabolinski, M. P.; Sobolewa, R. M., and others: Zur Frage der epidemiologischen Bedeutung der Weil-Felix-Reaktion bei Flecktyphus, Ztschr. f. Immunitätsforsch. u. exper. Therap. **81**:405-409 (Feb. 15) 1934.

roborative but not 100 per cent positive and that it is rarely positive one year after typhus.

The exanthin reaction [38] with Proteus X19 filtrate injected intracutaneously has been used in the acute stage of the disease and is usually negative after the seventh day.

The results of another cutaneous test [39] in which formaldehydized rickettsia bodies were used were reported previously. These and further results will be reported in detail. Intracutaneous injections have caused reactions in patients who were convalescing from typhus as early as two weeks after the disease and in those who had recovered from typhus as late as several years after the disease.

Gangrene as a Complication.—Gangrene is preeminent among the many complications following typhus. During a tremendous epidemic which swept from Russia over the entire European Continent, resulting in millions of deaths, Thomas Jordanus (1576) observed that the cardinal symptoms of typhus are "high fever, prostration and *gangrene*." Similar observations were made during the nineteenth century by von Hildebrand,[40] Blümm,[41] Deppisch,[42] Graber,[43] Aspelin,[44] Gregory [45] and Kagan.[46]

It is interesting to note that during the Serbian campaign of 1913 and 1914 and during the World War medical journals and lay periodicals commented on the prevalence of gangrene among the troops. Exposure, chilling and frost-bite were held responsible. At the same time a similar condition was not reported from any other war areas

38. Fleck, L., and Hescheles, I.: Ueber eine Fleckfieber-Hautreaktion (die Exanthinreaktion) und ihre Ähnlichkeit mit dem Dicktest, Klin. Wchnschr. **10**: 1075-1076 (June 6) 1931.

39. Goodman, C., and Brodie, M.: A Test for Diagnosis of Thrombo-Angiitis Obliterans, Proc. Soc. Exper. Biol. & Med. **32**:1331-1332 (May) 1935; Skin Test Indicating Previous Typhus Infection, ibid. **32**:1332-1334 (May) 1935. Goodman, C.: A Skin Test to Suggest the Diagnosis of Recovered Typhus and Thrombo-Angiitis Obliterans, Bull. New York Acad. Med. **11**:403-405 (June) 1935.

40. von Hildebrand, J. V.: Ueber den ansteckenden Typhus, Vienna, Camesina, 1815.

41. Blümm, H.: Ueber Gangrän nach Typhus, Inaug. Dissert., Würzburg, C. J. Becker, 1872.

42. Deppisch, A.: De gangræna typhum subsequente, Inaug. Dissert., Dorpat, H. Laakmanni, 1852.

43. Graber, C.: Gangrän der Extremitäten nach Typhus, Inaug. Dissert., Breslau, H. Lindner, 1869.

44. Aspelin, E. F.: Om gangrän uti nedra extremiteterna efter tyfus, Inaug. Dissert., Helsingfors, J. C. Frenckell & Son, 1868.

45. Gregory, A.: Chirurgische Erkrankungen als Komplikation nach Typhus exanthematicus und recurrens, Deutsche Ztschr. f. Chir. **181**:66-73, 1923.

46. Kagan, S.: Gangrene of the Foot as a Complication of Typhus Fever and Its Treatment, Boston M. & S. J. **189**:593-594 (Oct. 25) 1923.

where the climate was equally severe and the soldiers likewise suffered exposure. When this finding is taken into consideration in connection with the epidemic of typhus in southeastern Europe, it is highly suggestive of a relation between typhus and gangrene.

THROMBO-ANGIITIS OBLITERANS

Presenile gangrene is a vascular disease of young or middle-aged males, usually occurring in the extremities. The chief complaint is intermittent claudication. On examination there is usually diminution or absence of pulsation in one or more of the tibial arteries, and the temperature of the limb is lower than that of the unaffected extremity.

Sex.—Thrombo-angiitis obliterans is predominantly a disease of the male sex. McGrath [47] and others have attempted to account for this on the ground that the "female sex hormones" afford protection against the disease. It is well to remember, however, that both typhus and Brill's disease are particularly common among males. Brill's disease is most frequently found among workers in graineries and ports, where rats are found in large numbers and naturally the rat flea and the rat louse abound. Typhus is common in armies and prisons, where the population is largely male. Friedman mentioned as a reason why women are less often victims of thrombo-angiitis the fact that they lead more or less protected lives, while men are constantly exposed to infection of all kinds. The disease does occasionally occur in women. Trabaud and Mredden [47] reported the case of an Arabian girl, aged 20, in whom both feet and both hands were affected.

About forty years ago, as an intern at the Mount Sinai Hospital, I saw my first case of thrombo-angiitis obliterans, at a time when the disease was first appearing coincident with the arrival of numerous immigrants from Russia and central Europe. The disease was eventually recognized as that described by Winiwärter,[48] of Billroth's Clinic, in 1879 under the name of endarteritis obliterans.

Pathologic Picture.—Buerger's description is much like that of Winiwärter, who wrote that in the arteries proliferation of the intima occurs with the narrowing of the lumen; there is a coagulation of the blood with thrombotic formation, which becomes organized. Infiltration of the media appears later. Proliferation may be patchy and may not involve the entire circumference. New capillaries appear, with round cell infiltration of the media. The veins likewise show proliferation

47. Trabaud, J., and Mredden: Maladie de Léo Buerger chez une jeune fille musulmane, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:579-583 (April 6) 1931.

48. Winiwärter, F.: Ueber eine eigenthümliche Form von Endarteriitis und Endophlebitis mit Gangrän des Fusses, Arch. f. klin. Chir. **23**:202-226, 1879.

and elevations about the valves, infiltration extending to the media and adventitia and new capillary formation in the thrombus corresponding to canalization.

Buerger, who considered the term "thrombo-angiitis obliterans" a more accurate description of the condition, summarized his findings in these words:

> Most of the large arteries and sometimes the veins as well are obliterated over a large extent of their course. All stages in the occlusive change may occur in the various vessels of the extremity or in the same vessel in the different parts of its course. The closure of the vessel is affected by red obturating thrombi. These become organized, vascularized and canalized. Recent red thrombi may involve large portions of the arteries or veins and are not secondary to the gangrenous process. They may occur even when no gangrene is present. In short, we are dealing with lesions of considerable extent, apparently initiated by the formation of occlusive thrombi, chiefly in the arteries, but not confined to these, followed by organization and healing with an attempt at the production of sufficient collateral circulation.

My own observations on the living subject have been in accord with those of Buerger only so far as the type of lesion is concerned but not as to distribution. In a series of 17 cases of arteriovenous anastomoses in which surgical treatment was employed, I [49] found the femoral artery invariably more or less thickened and in several instances almost completely occluded, whereas the femoral vein, while showing some thickening of its wall, always retained its lumen.

It is a well established fact that presenile gangrene is a vascular constitutional disease, although it most frequently manifests itself in the vessels of the lower extremities. It is accepted that vascular complication arising in the course of other diseases, such as arteriosclerosis and diabetes, also manifests itself mainly in the lower extremities as a rule. In 1932 Jäger,[50] of Leipzig, published an article in which he describes the autopsy observations in 8 cases in which he found thrombo-angiitis obliterans in vessels other than those of the lower extremities. Taube,[51] of New York, described 2 cases in which he discovered the disease in the vessels of the abdomen. Cohen and Barron (1936) compiled from the literature reports of 15 cases of thrombo-angiitis obliterans suggesting involvement of the vessels of the alimentary tract. Only 4 of these were proved at autopsy. These authors presented an additional presumptive case.

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49. Goodman, Charles: Arterio-Venous Anastomosis for Impending Gangrene: A Report of Personal Experience with Fifteen Operated Cases, Tr. Internat. Cong. Med., London (sect. VII, pt. 2, Surg.), 1913, pp. 101-123.

50. Jäger, E.: Zur pathologischen Anatomie der Thrombangiitis obliterans bei juveniler Extremitätengangrän, Virchows Arch. f. path. Anat. **284**:526-622, 1932.

51. Taube, N.: Mesenteric Involvement in Buerger's Disease (Thrombo-Angiitis Obliterans): Report of Two Cases, J. A. M. A. **96**:1469-1472 (May 2) 1931.

Perla,[52] Dürck,[53] Lemann [54] and others reported finding thrombo-angiitis obliterans in the coronary artery. Recently Saphir [55] reported the results of postmortem examinations of the coronary arteries in a series of 30 cases of thrombo-angiitis obliterans collected from the literature. Lemann, who in 1928 described a similar case, emphasized the frequency with which coronary involvement occurs in this disease. Birnbaum, Prinzmetal and Connor [56] described a case of generalized thrombo-angiitis obliterans with involvement of the retinal vessels and adrenal infarction.

RELATIONSHIP OF TYPHUS TO THROMBO-ANGIITIS OBLITERANS

Epidemiologic Relation.—In considering the European environment, one fact stood out most conspicuously, namely, that typhus was constantly endemic and frequently epidemic in Russia and in certain mid-European areas. It was practically pandemic in the crowded Jewish quarters. In Russia the incidence of typhus, both virulent and mild, is high, while the incidence of thrombo-angiitis obliterans is also high.

Typhus is endemic in Russia, Siberia, Central Europe, Ireland and North Africa, in South America, especially in Chili and Peru, and in the United States, where it is known as Brill's disease. About 2,000 cases are reported annually in the United States. Likewise, thrombo-angiitis occurs in these areas.

Studies of Zinsser in New York indicate a close parallel between the incidence of thrombo-angiitis obliterans and that of typhus. From 1910 to 1933, of all the cases of typhus recorded in New York 97 per cent were in Jews, and 92.3 per cent of the afflicted Jews were of foreign birth. During the period 1921 to 1933, when a considerable portion of the total Jewish population of New York was of native birth, 91 per cent of all cases were in Jews, 85 per cent of whom were of foreign birth. Of the total of 538 cases of typhus occurring in New York and Boston during a thirty year period, 94.8 per cent were in persons of foreign birth. Of all the cases, over 97 per cent were

52. Perla, D.: An Analysis of Forty-One Cases of Thrombo-Angiitis Obliterans, with a Report of a Case Involving the Coronaries and the Aorta, Surg., Gynec. & Obst. **41**:21-30 (July) 1925.

53. Dürck, H.: Die sogenannte "Thrombangiitis obliterans" im Rahmen der infektiös-toxischen Gefässentzündungen, Verhandl. d. deutsch. path. Gesellsch. **25**: 272-289 (April) 1930.

54. Lemann, I. I.: Coronary Occlusion in Buerger's Disease (Thrombo-Angiitis Obliterans), Am. J. M. Sc. **176**:807-812 (Dec.) 1928.

55. Saphir, O.: Thromboangiitis Obliterans of the Coronary Arteries and Its Relation to Arteriosclerosis, Am. Heart J. **12**:521-535 (Nov.) 1936.

56. Birnhaum, W.; Prinzmetal, M., and Connor, C. L.: Generalized Thrombo-Angiitis Obliterans: Report of a Case with Involvement of Retinal Vessels and Suprarenal Involvement, Arch. Int. Med. **53**:410-422 (March) 1934.

in the Jewish racial group, and within this group 95 per cent were in the foreign-born members. The large percentage of Jews in these statistics merely means that the immigrants from typhus endemic areas to the United States consisted largely of Jews and the large percentage of Russians means almost entirely Russian Jews.

On the basis of these figures it might well be assumed that typhus, had it not been a well known disease with a world-wide incidence, might, like thrombo-angiitis obliterans, have been described as a predominantly Jewish disease. The fact that during the same period and in the same city the two diseases appeared almost simultaneously and almost exclusively in a racial group coming directly from the typhus centers of Russia and Central Europe is highly significant.

Both diseases have quiescent periods, and there may be recrudescences. Outbreaks of typhus vary considerably in virulence. Some infections gradually lose their virulence and finally disappear for an indefinite period or pass unrecognized. They then reappear in an intensely virulent form. This is particularly true when an infectious disease has prevailed for a great many years and the inhabitants have become more or less immune or when, as has been suggested, exposure to the disease has resulted in a very mild or unapparent form of the disease, which affords protective immunity.

Both diseases give rise to endothelial changes and thrombosis, with infiltration about the walls of the vessels.

In 1917 I attempted to reproduce the disease in guinea-pigs with injections of blood from patients with typhus. Microscopic study of the vessels of the hindlegs showed changes analogous to those seen in thrombo-angiitis obliterans.

In 1922 Wolbach published an exhaustive monograph of his studies on typhus in Poland. He mentioned thrombosis engendered by the presence of rickettsias in the endothelium. At that time I had under my care a number of patients with gangrene in the advanced stage which necessitated amputation. I prevailed on Dr. Klein, the pathologist of the Montefiore Hospital, to look for rickettsia-like bodies in the vessels which I had dissected from the amputated limbs. He reported that he found bodies like those described by Wolbach, but he did not attempt to grow them because no method for tissue culture existed at that time. Dr. Seecof, working independently and without the knowledge of Dr. Klein's findings, also discovered bodies which resembled Wolbach's microscopic picture of Rickettsia in material from thrombo-angiitis obliterans patients.

EXPERIMENTAL WORK AND RESULTS

The recent studies of Zinsser concerning the possible relationship of Brill's disease to a previous typhus infection suggests the impor-

tance of determining by a simple test a previous infection with typhus. We proceeded, therefore, to attempt to establish further identity between the two conditions by a cutaneous test.

The purpose of the test is to determine: (1) whether with a formaldehydized preparation of rickettsia bodies a reaction can be observed in persons who have recovered from typhus; (2) whether cutaneous reactions can be obtained in persons with thrombo-angiitis obliterans, and (3) whether any cutaneous reaction obtained is quantitative or qualitative.

A few efforts have been made by others to devise a cutaneous test. For example, Jacobsthal [57] in 1916 made a louse extract from typhus-infected lice in which the virus was killed. Intracutaneous inoculation gave a positive reaction in patients with acute typhus, but the procedure was entirely too complicated to be of practical value. Friedberger, Sparrow and Delanoë used a small amount of Proteus X19, but this test gave a positive reaction in cases of typhoid and relapsing fever as well and hence was of little diagnostic value. Bogdanoff,[58] Fleck and Krukowsky devised a modified exanthin test which they claimed was specific for typhus during the first week. In the convalescent period the reactions of 80 per cent of the patients became negative, and positive results were observed in healthy persons. This reaction, therefore, could not take the place of the Weil-Felix reaction.

In several former publications I have described the test which I devised, using a formaldehydized vaccine supplied through the courtesy of Dr. Hans Zinsser, of the Department of Bacteriology and Immunology of the Harvard University.

Technic for Cutaneous Test.—The technic consists of an intracutaneous injection of from 0.1 to 0.2 cc. of the vaccine on the palmar aspect of the forearm. For control tests, Proteus X19 filtrate and a formaldehydized suspension of tunica vaginalis from healthy guinea-pigs were used as well as a suspension of streptococci and staphylococci.

For these tests three groups of persons were selected: (1) patients with thrombo-angiitis obliterans, (2) persons convalescent and recovered from typhus and Brill's disease and (3) normal persons.

Experiment 1.—The first group tested consisted of 20 patients. The results, which have already been reported, are as follows: All of these patients had a history of Brill's disease from six to eight years previously, and in all but 1 case the diagnosis at that time had been confirmed by the Weil-Felix reaction. For controls, 22 adults with no previous history of typhus were given similar tests with the suspension of rickettsia. These patients were observed for from twenty-four to forty-eight hours after the injections were given. The results are given in table 1. None of the 22 controls gave any reaction, whereas all of the 20 with

57. Jacobsthal, E.: Eine Anregung zur Anstellung von Kutisreaktion bei Fleckfieber, Deutsche med. Wchnschr. **42**:1093-1094 (Sept. 7) 1916.

58. Bogdanoff, I. L.: Ueber eine intrakutane Reaktion beim Flecktyphus, Zentralbl. f. Bakt. (Abt. 1) **128**:173-177 (April 28) 1933.

a history of previous typhus infection showed an erythematous indurated area from 1 to 4 cm. in diameter at the end of twenty-four hours. Another person similarly tested two weeks after convalescence likewise had a reaction 2 cm. in diameter.

These results suggest that patients who have recovered from typhus display a sensitivity to rickettsia bodies and that this sensitivity persists for a considerable period of time.

EXPERIMENT 2.—In a second group of 32 adults with thrombo-angiitis obliterans, some with and others without gangrene, the tests with a formaldehydized suspension of rickettsia were similarly made. These showed without exception a 1 plus or a 2 plus reaction. (An erythematous area from 0.5 to 2 cm. in diameter was recorded as 1 plus, and anything larger was recorded as 2 plus.) For control tests, Proteus X19 filtrate was used on 9 of these patients, a suspension of tunica vaginalis from healthy guinea-pigs on 9 and a suspension of staphylococci and a suspension of streptococci on 9 and 6, respectively. All of the patients showed a negative reaction, with the exception of those having ulceration or gangrene. In 1 of the patients in the latter group the reaction to the streptococcus vaccine was positive, while in 4 the reaction to the staphylococcus vaccine was positive.

TABLE 1.—*Results in Experiment 1*

Subjects	Number of Persons	Reaction to Suspension of Rickettsia (Zinsser No.1)	Reaction to Proteus X19 Filtrate	Reaction to Suspension of Tunica Vaginalis
Persons recovered from typhus..	20	20+	20—	20—
Control subjects.....	22	22—	22—	22—

A series of 11 adults with arteriosclerosis and others with diabetes, some with and others without gangrene, responded negatively both to tests with rickettsias and to control tests, excepting 2 with gangrene in whom the cutaneous reaction to the staphylococcus vaccine was positive.

Preparation of Vaccines.—At this time preparation for the production of vaccine in the laboratory of the New York University was undertaken. This was made possible through the courtesy of Dr. W. H. Park.

These vaccines were prepared according to Dr. Zinsser's technic and carried out with the assistance of Mr. George J. Stein. We inoculated guinea-pigs and rats passed through several generations in order to obtain the maximum number of rickettsias.

Material for the initial inoculations was derived from a tissue culture strain furnished us through the courtesy of Dr. Landsteiner, of the Rockefeller Institute, as well as from guinea-pigs inoculated with Mexican typhus furnished us by Dr. Zinsser. Another European tissue culture furnished us by Dr. Landsteiner was passed through several generations of pigs, and a brain emulsion was prepared. To this group of Mexican typhus vaccine and the European virus, we were able to add a European typhus vaccine prepared for me by Professor Weigl, of Poland.

Mexican Typhus Vaccine.—With the cooperation of Dr. Ira I. Kaplan, of the Bellevue Hospital, rats were irradiated with a dose of 700 roentgens and immediately inoculated intraperitoneally with an emulsion of tunica vaginalis from guinea-pigs infected with Mexican typhus. Five days after inoculation each rat was killed

by a blow on the head, dipped in compound solution of cresol to kill all lice, shaved and put on a board. The peritoneal lining and tunica vaginalis were removed. These were washed several times in sodium citrate to which a 0.2 per cent concentration of solution of formaldehyde U. S. P. had been added. They were pooled and washed again several times. They were then centrifugated fractionally. The residue was ground with sand and centrifugated again and again until purified and rendered free as possible from cellular detritus.

We then received a third supply of vaccine from Dr. Zinsser. At first the results with this vaccine were disappointing as we observed reactions in presumably normal persons. Experiments were therefore undertaken to determine the reason.

EXPERIMENT 3.—The vaccine was heated for thirty minutes at 70 C. in a water bath. The results were not encouraging.

TABLE 2.—*Results with N. Y. U. Vaccine 1, 2 and 3* *

Subjects	N. Y. U. 1	N. Y. U. 1 Heated	N. Y. U. 1 (120,000,000 to 170,000,000)	N. Y. U. 2 (150,000,000)	N. Y. U. 3 (150,000,000)
Persons with thrombo-angiitis obliterans	7+ 1—	1+ 1—	61+ 1—	20+ 2—	14+
Control subjects	8— 1+	7— 7+	16— 3+	18— 1+	5—

* N. Y. U. vaccine refers to the vaccine prepared in the laboratory of New York University.

TABLE 3.—*Comparative Results with Weigl and with N. Y. U. Vaccine*

Subjects	Weigl (140,000,000)		N. Y. U. 1 (120,000,000 to 150,000,000)		N. Y. U. 2 (140,000,000 to 150,000,000)		N. Y. U. 3 (140,000,000 to 150,000,000)	
Persons with thrombo-angiitis obliterans	26+	100%	37+ 1—	97% 3%	20+ 2—	91% 9%	14+	100%
Control subjects	14—	100%	8—	100%	18— 1+	95% 5%	5—	100%

EXPERIMENTS 4, 5, 6 and 7.—Tests were carried out with dilutions 1:4, 1:6, 1:7 and 1:10, respectively. With the higher dilutions, the reactions proved more consistently uniform in patients with typhus and in those with thrombo-angiitis and negative in the controls.

EXPERIMENTS 8, 9 and 10.—Similar tests were made with dilutions of vaccine with batches 4, 5 and 6 prepared in our laboratory and carried out after the preliminary results with the third batch of vaccine from Dr. Zinsser.

Results with these various vaccines at our command indicated that each product must vary in the quantity of its essential ingredient. It became evident that a standardized preparation was necessary to render the tests of practical value.

The streptococci and staphylococci used for our control test had been labeled at their source and identified by the number of bacteria contained in each cubic centimeter. It occurred to me, therefore, to apply the same principle for our rickettsia vaccines. The vaccines prepared by us as well as that obtained from Dr. Zinsser and the European

strains made from typhus-infected lice furnished us by Professor Weigl were titered. We made use of the standardization measure of counting against normal red blood cells. We found that the batches of vaccine varied considerably in the number of rickettsias contained, namely, from 828,000,000 to 2,200,000,000 rickettsias to a cubic centimeter. The emulsion of the brains of guinea-pigs prepared from the European culture obtained from Dr. Landsteiner did not lend itself to titrating.

TABLE 4.—*Experiments and Results with Eight Different Batches of Vaccine and Control Tests*

	Persons with Thrombo-angiitis Obliterans	Persons with Typhus	Control Subjects
Zinsser No. 1	12+	25+	13— 1+
Zinsser No. 2	21+	13+	3—
Zinsser No. 3	9+ 1—	13+ 2—	2— 2+
Zinsser No. 3 (heated)	5+	1+	
Zinsser No. 3, 1:4	9+ 2—	9+ 2—	5— 1+
Zinsser No. 3, 1:4 (heated)	11+ 4—	15+ 6—	24— 2+
Zinsser No. 3, 1:10	7+ 8—	3+ 4—	7— 1+
Zinsser No. 3 (140,000,000)	.....	4+ 1—	
Proteus X19 filtrate	5—	5—	3—
Tunica vaginalis	19—	22—	7—
Weigl	12+ 2—	12+ 2—	
Weigl (heated)	1+	1+	3— 1+
Weigl, 1:4	11+ 4—	17+ 4—	10— 3+
Weigl, 1:4 (heated)	23+ 4—	24+ 5—	14— 2+
Weigl (140,000,000)	26+	9+ 1—	17—
N. Y. U. 1	7+ 1—	2+	8— 1+
N. Y. U. 1 (heated)	1+ 1—	2+ 1—	7— 7+
N. Y. U. (170,000,000)	34+ 3—	47+ 1—	4— 2+
N. Y. U. (150,000,000)	12+	3+	1+
N. Y. U. (120,000,000)	25+ 1—	28+ 3—	8—
N. Y. U. (100,000,000)	5+ 5—	1+ 2—	4—
N. Y. U. 2	6+ 2—	2+	
N. Y. U. (150,000,000)	8+ 1—	6+	6—
N. Y. U. (140,000,000)	12+ 1—	33+ 1—	12— 1+
N. Y. U. (100,000,000)	3+ 2—	2—	
N. Y. U. 3	.....	.....	.....
N. Y. U. (150,000,000)	8+	4+ 1—	5—
N. Y. U. (140,000,000)	6+	10+ 6—	
N. Y. U. (100,000,000)	1+		
N. Y. U. European vaccine 1:10	3+ 1—	1—	7—
Staphylococci	5+ 7—	3+ 4—	8— 3+
Streptococci	9+ 7—	5+ 4—	9—
N. Y. U. 1, 2 and 3 (pooled)	.....	4+	2—

In the course of our experiments we have made over 600 intradermal tests with suspensions of Rickettsia Prowazeki and control material in the following subjects: 96 patients convalescing or recovered from Brill's disease (or typhus); 94 patients with thrombo-angiitis, and over 100 controls.[58a] These controls included a series of presumably normal persons and persons with arteriosclerosis, diabetes, typhoid, pneumonia, scarlet fever, bacterial endocarditis, intestinal tuberculosis and other acute infectious conditions.

58a. These tests were made possible through the cooperation of the staff of the Brooklyn Jewish Hospital.

We found that an intracutaneous injection of 0.1 cc. of suspension containing approximately 150,000,000 rickettsias per cubic centimeter will be followed in cases of thrombo-angiitis obliterans by a reaction demonstrated within twenty-four hours by an erythematous area from 0.5 to 4 cm. in diameter. This usually disappears in the course of another twenty-four hours. In our series of controls these tests proved almost invariably negative. The summary of the results with the various preparations and their dilutions is given in the tables. Of interest was the observation in the course of our examination of the series of patients with Brill's disease. A considerable number of those complained of persistent and frequent headache as well as pains in the lower extremities, including intermittent claudication. Among these, there came to our notice 11 persons with a history of at least two attacks of typhus with an interval of several years, as well as one who had had typhus no less than three times. An examination of the extremities of these persons disclosed absence of pulsation in one or more of the tibial arteries with an appreciable difference in the amplitude of one extremity as compared with the other, as demonstrated by the oscillometer. These patients portrayed subjective and objective findings suggestive of thrombo-angiitis obliterans. Several of them gave a history of never having smoked or used tobacco.

COMMENT

Since I was first impressed in 1916 by the possible etiologic relationship of typhus to thrombo-angiitis obliterans, the same idea has suggested itself to Netter,[59] in 1932. Similar opinions have been expressed by Troisier and Horowitz,[60] who reported a case in which the Weil-Felix reaction was intensely positive in a 23 year old man with Buerger's disease, while in 7 controls the reaction was negative. Angelescu, Georgescu and Buzoianu,[61] on the basis of observations made in Roumania, stated that they have been impressed by the possibility that exanthematous typhus may be a factor in the production of chronic obliterating arteritis.

From the foregoing review, the test outlined, the epidemiologic evidence, the pathologic similarity and the facts that in a considerable proportion of patients with typhus clinical evidence of thrombo-angiitis

59. Netter, A.: Nécessité de la recherche des manifestations inapparentes du typhus endémique chez les matelots des équipages de Toulon, Bull. Acad. de méd., Paris **107**:156-158 (Feb. 9) 1932.

60. Troisier, J., and Horowitz, A.: Maladie de Buerger et typhus exanthématique, Bull. et mém. Soc. méd. d. hôp. de Paris **57**:151-157 (Feb. 3) 1933.

61. Angelescu, C.; Georgescu, G., and Buzoianu, G. V.: Exanthematous Typhus as an Etiologic Factor in Chronic Arteriitis Obliterans, Spitalul **50**:401-402 (Nov.) 1930.

obliterans develops and that the cutaneous test is positive in persons with typhus as well as in persons with thrombo-angiitis obliterans, it appears that there is a relation between the two diseases.

SUMMARY

Of the various agents that have been suspected of having an etiologic relation to thrombo-angiitis obliterans, none have thus far given any substantial evidence to support the suspicion. Thrombo-angiitis obliterans is a disease not confined to any one race or locality. Like typhus and the typhus-like fevers, its occurrence is widespread.

A study of the epidemiology of these diseases shows that where one of them is common the other is also abundant. Gangrene of the extremities is an outstanding complication of typhus, being a more frequent sequela of typhus than any other infection. Those who have made a thorough study of thrombo-angiitis obliterans agree that it is a constitutional disease of infectious origin. On the basis of these facts I developed the thesis that typhus bears a definite etiologic relation to thrombo-angiitis obliterans. In support of this thesis I present certain highly suggestive evidence. I first devised a cutaneous test which gives a positive reaction over a prolonged period in persons who have had typhus. This test is almost uniformly positive in persons who have had typhus or Brill's disease and almost uniformly negative in normal persons. In a group of adults with thrombo-angiitis obliterans the test was almost uniformly positive, while in a group with arteriosclerosis and diabetes it was negative.

The findings in these series of tests are highly suggestive of an etiologic relation between typhus and thrombo-angiitis obliterans. They open the way for further research, and they justify the hope that eventually an immunologic agent may be found which will inhibit the development of thrombo-angiitis obliterans.

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ALTERATIONS IN THE HIP JOINT AFTER DEAFFERENTATION

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In studying the effect of lumbar sympathectomy and section of the lumbosacral dorsal roots on the structure of bones and joints in adult cats, a condition closely simulating the arthritic changes in malum coxae senilis of man was found in deafferented hip joints.

The numerous experimental procedures on animals, such as the rabbit, dog, cat and guinea-pig, which have resulted in conditions simulating arthritis deformans in man were reviewed by Burckhardt,[1] Mannheim [2] and Key.[3] These experiments usually included intracapsular traumatization or destruction of a portion of the articular cartilage and resulted in the acceptance by many of the thesis that degeneration of articular cartilage is a primary condition in the production of the senile type of chronic hypertrophic arthritis in man. Axhausen [4] has been the foremost exponent of this concept. From his experimental work on dogs, Wollenberg [5] concluded that degenerative alterations in a joint are primarily due to changes in the blood supply to that joint and that atrophic and hypertrophic changes may be explained on the basis of localized ischemia and hyperemia, respectively. On the other

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1. Burckhardt, H.: Experimentelle Untersuchungen über die Beziehungen der Gelenkfunktion zur Arthritis deformans, Arch. f. klin. Chir. **132**:706, 1924.

2. Mannheim, A.: Experimentelle Arthritis deformans, Arch. f. klin. Chir. **156**:334, 1930.

3. Key, J. A.: Experimental Arthritis, Chronic and Atrophic, M. J. & Rec. **138**:369 (Nov. 15) 1933.

4. Axhausen, G.: Kritisches und Experimentelles zur Genese der Arthritis deformans, insbesondere über die Bedeutung der aseptischen Knochen- und Knorpelnekrose, Arch. f. klin. Chir. **94**:331, 1911; Ueber einfache, aseptische Knochen- und Knorpelnekrose, Chondritis dissecans und Arthritis deformans, ibid. **99**:519, 1912; Neue Untersuchungen über die Rolle der Knorpelnekrose in der Pathogenese der Arthritis deformans, ibid. **10**[illegible]:301, 1914.

5. Wollenberg, G. A.: Aetiologie der Arthritis deformans, Ztschr. f. orthop. Chir. **24**:359, 1909.

hand, Lane [6] attributed such changes to pressure, while Meyer [7] emphasizes the fact that certain changes in the joints in man may result from trauma of use and that synovial bursae, articular cartilages, capsules and tendons frequently show changes which suggest that they were produced solely by attrition in otherwise normal joints. It is interesting that Virchow and Fränkel [8] in considering changes in the joints in tabes dorsalis and arthritis deformans attributed the defects in the cartilage and bony polishing to the mechanical trauma of friction, but never on intact normal cartilage, always on hyperplastic softened cartilage.

In attempting to determine the pathogenesis of Charcot joints, Eloesser [9] sectioned the lumbosacral dorsal roots in a large series of cats. In active animals which used their deafferented limbs considerably he found changes in the joints that were highly characteristic of those seen in the neuropathic arthropathies. He concluded that the cause of these deformed joints was altered function, due to insensibility of the joints.

MATERIAL AND METHODS

In the experiments reported here, fifteen cats were used. The lumbar sympathetic chain was excised bilaterally in seven animals and unilaterally in eight. The fourth, fifth, sixth and seventh lumbar dorsal roots and the first, second and third sacral dorsal roots were also sectioned unilaterally on the side of the sympathectomy, in four of the cats before and in nine after, sympathectomy. In two of the animals unilateral sympathectomy was not followed by deafferentation. The interval between these operations varied from two weeks to one year; that between sympathectomy and autopsy varied from one hundred and twenty-seven to one thousand and ninety-seven days, and that between deafferentation and autopsy, from fourteen to one thousand, one hundred and fifty-eight days.

Ether anesthesia was used in all of the operative procedures, and the animals were watched carefully to prevent the development of traumatic ulcers of the skin. Ten of the cats were permitted to run freely in a large outdoor cage, about 8 by 10 feet (2.4 by 3 meters), and five were kept in relatively small standard animal cages, 1½ by 2 feet (0.45 by 0.6 meter). As will be seen later, this difference in the range of activity undoubtedly played a part in the absence or presence of the articular changes.

Roentgenograms were made of the entire lower extremity of each animal before autopsy and after fixation and cleaning of the bones. Careful macroscopic and

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7. Meyer, A. W.: Further Observations upon Use-Destruction in Joints, J. Bone & Joint Surg. **4**:491, 1922; Evidences of Attrition in the Human Body, Anat. Rec. **25**:142, 1923; Further Evidences of Attrition in the Human Body, Am. J. Anat. **34**:241, 1924; The Minuter Anatomy of Attrition Lesions, J. Bone & Joint Surg. **13**:341, 1931.

8. Virchow, R., and Fränkel, B.: Berliner medicinische Gesellschaft, Berl. klin. Wchnschr. **23**:851, 1886.

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microscopic examinations of the bones were made after fixation in diluted solution of formaldehyde U. S. P. (1:10), the histologic studies being made on bones decalcified in a 5 per cent aqueous solution of nitric acid and embedded in pyroxylin. The craniocaudal and dorsoventral diameters of the heads of the femurs were measured. The femurs, patellae, tibias and fibulas of five animals were cleaned of all soft parts, dried in the oven at 110 C., then placed in a number of changes of ether to remove the fat and again dried at 110 C. until a constant weight was obtained. In all animals the normally innervated limb or its component parts served as a control.

RESULTS

The bones and joints of the two animals on which lumbar sympathectomy only was performed showed no changes after two years, but the hip joints of animals which used their deafferented limbs considerably showed alterations. Except for the slight increase in the weight

TABLE 1.—*Weight of Bones After Drying and Extraction with Ether*

Cat	Days Separating Operation and Autopsy: Sympathectomy	Days Separating Operation and Autopsy: Deafferentation	Bones	Weight of Bone on Normal Side, Gm.	Weight of Bone on Side Operated On, Gm.	Difference, Gm.
238	1,029	728	Femur	7.02	7.84	+0.82
			Patella	0.33	0.34	+0.01
			Tibia	6.60	7.20	+0.60
			Fibula	0.89	0.87	−0.02
421	379	350	Femur	6.50	6.97	+0.47
			Patella	0.27	0.26	−0.01
			Tibia	5.44	5.43	−0.01
			Fibula	0.72	0.95	+0.23
276	672	1,000	Patella	0.29	0.32	+0.03
			Tibia	6.87	7.36	+0.49
			Fibula	0.88	1.10	+0.22
277	794	1,008	Patella	0.54	0.52	−0.02
			Tibia	9.90	10.00	+0.10
			Fibula	1.22	1.24	+0.02

of the bones in the deafferented limbs (table 1) and the changes in the hip joints, no alterations were noticed in the denervated bones. It is significant that the increase in weight in the affected bones roughly paralleled the extent of the deformation.

The manner in which the deafferented hindlimb was carried is illustrated in figure 1. It was extended at the hip and knee, the dorsum of the foot dragging along the ground. Although the cat shown in figure 1 carried the left hindlimb in an abducted position, most of the cats carried it in adduction. The deafferented limb offers less support than the normal limb, causing the pelvis to tilt toward the denervated side and bringing that leg into adduction. Adduction and abduction increase tension on the upper and lower portions, respectively, of the capsule, which if prolonged permits an increase in the range of movement of the joint. This hypermobility permits excessive wear on portions of the articular surface unadapted to it, in joints the proprio-

ceptive sense of which has been abolished, and prevents maintenance of the normal position.

The roentgenogram of the hind part of a cat on which deafferentation was performed one thousand, one hundred and fifty-eight days previously and sympathectomy seven hundred and thirty-six days previously is shown in figure 2. Subluxation of the head of the femur toward the iliac surface is present on the left. The acetabular fossa appears very shallow, and an increase in the density of the spongiosa of the head and neck of the femur is indicated. This increase in density extends even into the cortex of the bone. The change in the head of the femur is more apparent in figure 3, which is a roentgenogram of the fresh stripped bones of the hindlimbs of the cat shown in figure 2, but

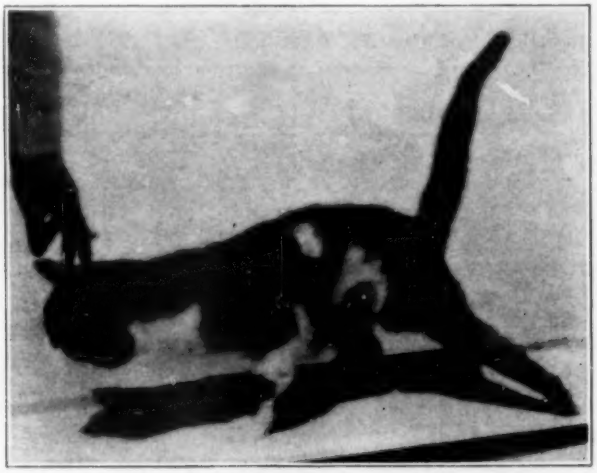

Fig. 1.—Photograph of cat 238 showing extension and abduction of the deafferented (seven hundred and twenty-eight days) and sympathectomized (one thousand and twenty-nine days) hindlimb. The dorsum of the foot is dragging on the ground.

reversed in position. There are marked increase in density, flattening of the weight bearing portion and an increase in the diameter of the head of the femur.

The weights of the dried femurs, patellae, tibias and fibulas of four of the cats are given in table 1. Marked arthritic changes were found in the hip joint of cat 238. The femur and the tibia of the deafferented limb were heavier than those of the normal limb, the difference in weight being greater than those between the bones in deafferented limbs of animals without alterations in the hip joints. It is surprising that this increase in weight was present also in the deafferented tibias. The femurs on the sides with marked changes in the hip joints always were

slightly heavier than those from the normally innervated limbs when weighed devoid of soft parts but without drying. The bones used for microscopic study could, of course, not be subjected to drying.

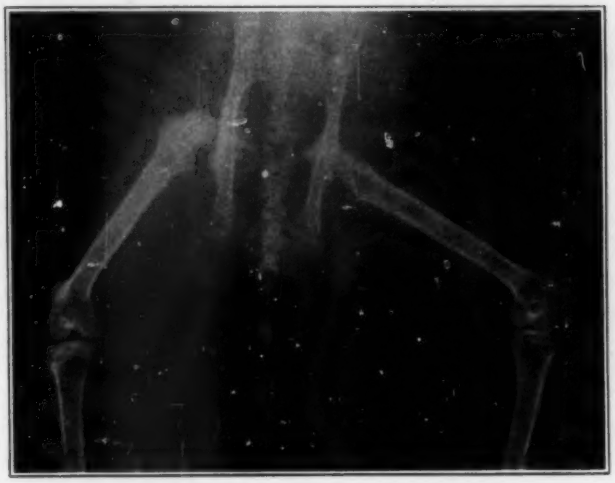

Fig. 2 (cat 216).—Roentgenogram of the posterior portion of the body of a live cat with a deafferented (one thousand, one hundred and fifty-eight days) and sympathectomized (seven hundred and sixty-three days) leg. There are subluxation of the hip and an increase in density of the head and the shaft of the femur on the left.

Fig. 3 (cat 216).—Roentgenogram of the cleaned bones of the hindlimbs. There is an increase in the diameter and density of the head of the femur on the right. This roentgenogram has been reversed in respect to figure 2.

The craniocaudal and dorsoventral diameters of the normal and the altered heads of the femurs are given in table 2. A notable difference

between the measurements on the two sides was seen in all animals except cat 277, in which only slight gross changes were found in the denervated hip joint. This cat did not move about as much as the others, although all were free in the large outdoor cage previously mentioned. The femurs from cats which were considerably restricted in their movements showed no alterations roentgenographically five hundred and fifty days after deafferentation. These cats are under observation and have not yet been killed.

The gross appearance of the femurs and coxal bones from paired hindlimbs of the same animal only one of which was denervated is shown in figure 4. Those on the right present a picture similar to hypertrophic arthritis. The hyaline articular cartilages are completely worn off from considerable portions of the apposed upper surfaces, where marked bony polishing is present. Enlargement of the affected head and acetabular fossa, synovial fraying and noticeable thickening of the capsule about the acetabular margin also are evident.

TABLE 2.—*Dorsoventral and Craniocaudal Diameters of Heads of Femurs*

	Normal Side		Side Operated On	
Cat	Dorsoventral Diameters, Cm.	Craniocaudal Diameters, Cm.	Dorsoventral Diameters, Cm.	Craniocaudal Diameters, Cm.
216	1.10	1.10	1.40	1.25
276	1.09	1.05	1.12	1.10
236	1.02	1.00	1.10	1.09
288	1.15	1.18	1.22	1.22
238	1.08	1.05	1.10	1.10
277	1.23	1.23	1.24	1.23

The appearance of the articular cartilage and the underlying spongiosa of the head of the femur from the normally innervated limb is shown in frontal section in figure 5. The normal hyaline cartilage, the compacta and the wide medullary spaces in the spongiosa are shown clearly. A similar section taken near the capitular fossa from the head of the femur of cat 277, on which deafferentation was performed one thousand and eight days previously and sympathectomy seven hundred and thirty-four days previously, is shown under somewhat lower magnification in figure 6. Here the cartilage is thicker than that shown in figure 5, as the two sections are not from corresponding areas of the joint capsule. For some reason this animal did not move about much. No roentgenographic changes were found in the bones, and only the slightest sign of wear of the cartilage was grossly evident in the region represented. However, detritus and superficial erosion and degeneration, with deeper striation or so-called fibrillation, were present in the cartilage. There was no sclerosis of the spongiosa.

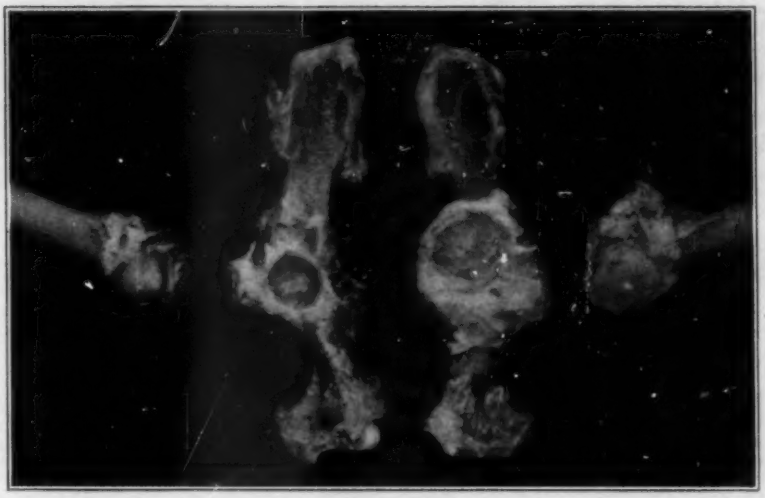

Fig. 4 (cat 216).—Paired femurs and coxal bones. The denervated coxal bone and head of the femur on the right show widening, erosion and bony polishing of both articular surfaces. Synovial tags are present on the inner surface of the thickened capsule; × 0.55.

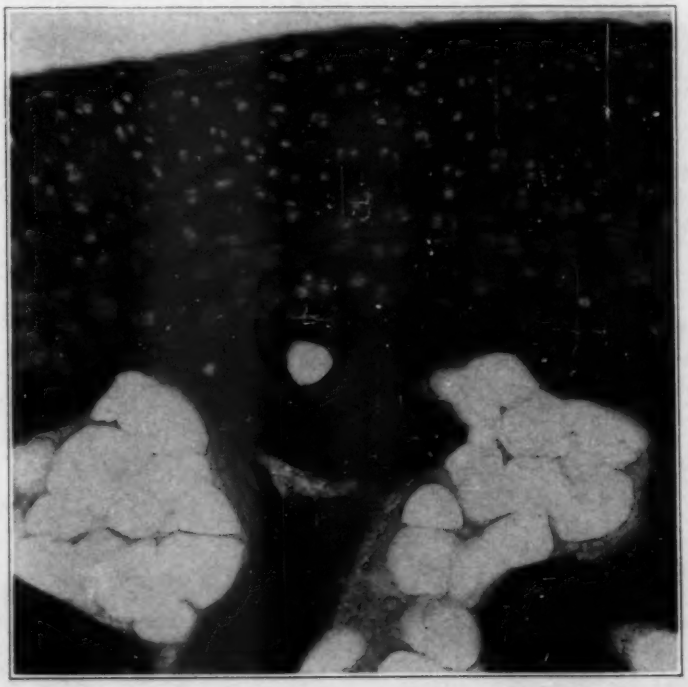

Fig. 5.—Photomicrograph of a frontal section of the articular surface of the head of the femur of a normally innervated limb; × 110. The cartilage and spongiosa are normal in appearance.

More pronounced changes are shown in figure 7, a section of the head of the femur from cat 288, on which deafferentation was done nine hundred and thirty-three days previously and sympathectomy seven hundred and thirty-two days previously. The calcified layer seems to be intact and cellular, although the underlying spongiosa shows evident signs of new bone formation by the presence of bony sclerosis or so-called eburnation. On comparing this figure with figure 5, it is evident that the medullary spaces are being reduced and that haversian systems are being formed in the spongiosa, producing a thickened

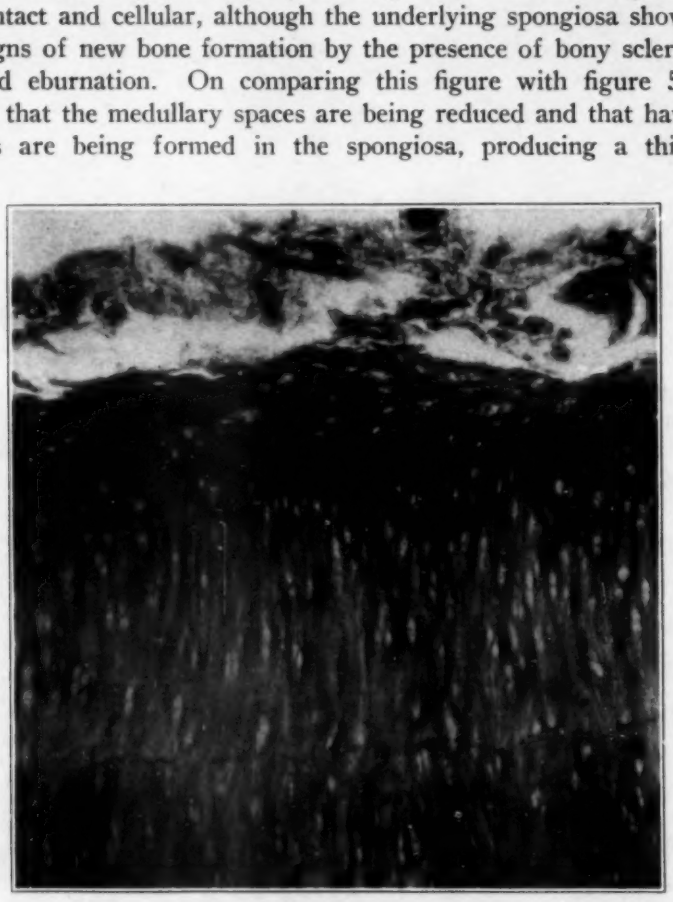

Fig. 6 (cat 277).—Photomicrograph of a frontal section of the articular surface near the capitular fossa of the head of the femur of a deafferented (one thousand and eight days) and sympathectomized (seven hundred and thirty-four days) hindlimb; × 100. There is superficial detritus with striation of the hyaline cartilage.

compacta. This suggests that the eburnation probably is a functional response and does not require removal of the calcified cartilage from the underlying compacta and direct mechanical stimulation.

A still more pronounced stage of this condition is shown in figure 8, a photomicrograph of a section from the head of the femur from a denervated hindlimb of cat 236 under low power magnification. The

cartilage is completely worn away from a large area of the head of the femur. A remnant of ligamentum teres, which was always destroyed in these cases of marked alterations in the joints, is seen at *l. t.* Bony sclerosis is present throughout the head but is most marked directly beneath the bare area. On the right of this figure one can see the extension of newly formed cartilage marginally and endochondral ossification extending into it. Deafferentation was done seven hundred and thirty-one days, and sympathectomy one thousand and ninety-seven days, previous to the death of the cat.

Fig. 7 (cat 288).—Photomicrograph of a frontal section of the head of the femur of a deafferented (nine hundred and thirty-three days) and the sympathectomized (seven hundred and thirty-two days) hindlimb; × 110. There are degeneration and destruction of the uncalcified hyaline cartilage and sclerosis of the spongiosa. The calcified cartilage is still intact.

A cross-section of the acetabulum from this animal, the head of the femur of which is shown in figure 8, is represented in figure 9 under low power magnification. There is pronounced marginal synovial fraying, and the hyaline articular cartilage on the left has been worn away for a distance of about 2 mm. All of the cartilage is destroyed, and the underlying spongiosa is eburnated. The right hand portion of

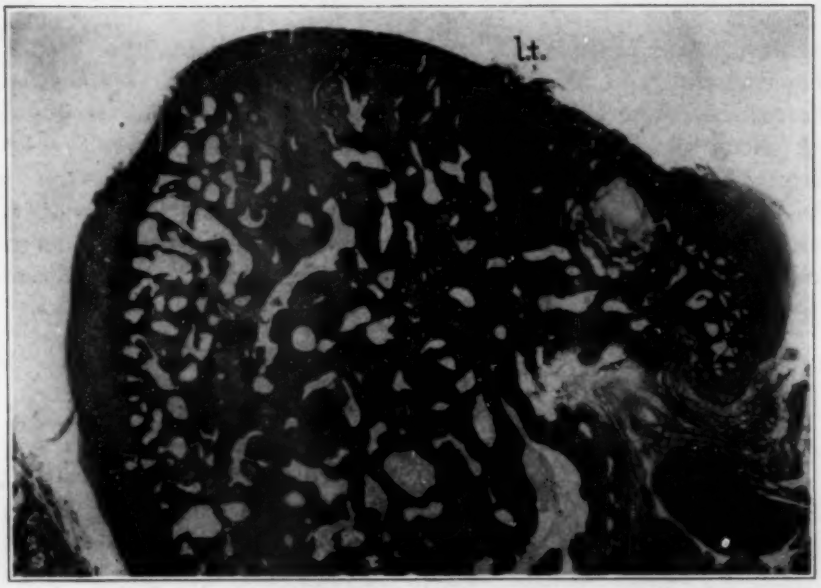

Fig. 8 (cat 236).—Photomicrograph of a frontal section from the head of the femur of a deafferented (seven hundred and thirty-one days) and sympathectomized (one thousand and ninety-seven days) hindlimb; × 12. The remnant of the ligamentum teres is indicated by *l.t.* The cartilage is completely worn away from a large area of the articular surface. There are bony sclerosis throughout the head and new cartilage formation on the right, with endochondral ossification extending into it.

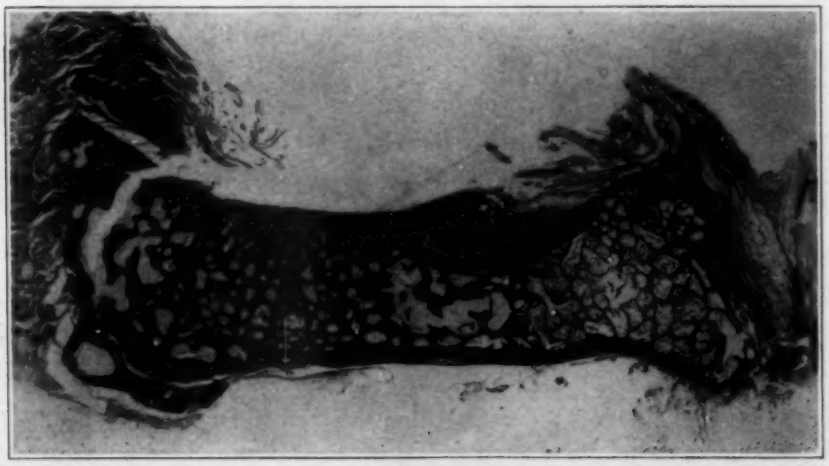

Fig. 9 (cat 236).—Photomicrograph of a cross-section of the acetabulum from the same deafferented limb shown in figure 8; × 5. The articular cartilage on the left is completely destroyed, and the surface of the joint is worn. There is sclerosis of the spongiosa on the left. The surface of the joint on the right is covered with new fibrocartilage in which endochondral ossification is taking place. There is no sclerosis in the spongiosa on the right, and synovial tagging and fraying are present.

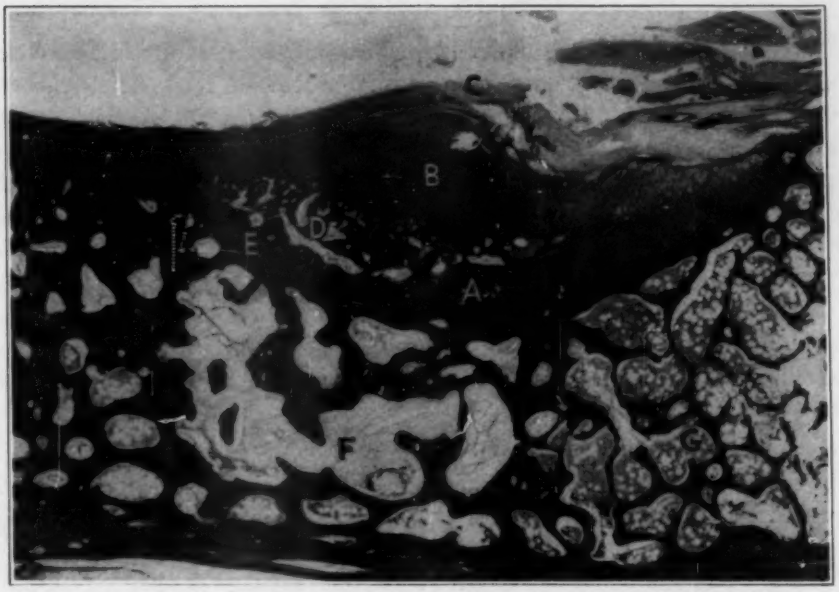

Fig. 10.—Photomicrograph of the same section shown in figure 9; × 12. *A* indicates hyaline cartilage of a former articular surface; *B*, new fibrocartilage continuous with the synovial membrane at *C*; *D*, a region in which endochondral ossification is taking place; *E*, a calcified cartilage zone; *F*, a large fibrous area in the medullary cavity, and *G*, normal-appearing medullary spaces and spongiosa.

Fig. 11 (cat 216).—Photomicrograph of a section of the synovial membrane from the hip joint from a deafferented (one thousand, one hundred and fifty-eight days) and sympathectomized (seven hundred and sixty-three days) hindlimb. There are numerous synovial villi and no evidence of inflammation.

this acetabulum is shown under higher magnification in figure 10. The old joint surface at *A* is covered with fibrocartilage, *B*, directly continuous with the synovial membrane at *C*. At *D*, endochondral ossification has taken place, apparently in the proximity of vascular loops, which appear to have penetrated the calcified cartilage at *E*. A large fibrous area is seen in the marrow at *F*, but the spongiosa at *G* is normal and contrasts markedly with that on the left under the denuded surface.

A section of the synovial membrane from a similar hip joint is shown in figure 11. Numerous synovial tags are present, but there is no evidence of an inflammatory reaction in this or in the other joints showing these changes, and the blood vessels appear normal in distribution and size.

COMMENT

Bony sclerosis or eburnation has been thought to result from the presence of necrotic cartilage or bone (Axhausen [4]), from a hyperemic condition of the medullary spaces (Wollenberg [5]), from a sclerosing osteitis (Knaggs [10]) or in compensation to "cartilage erosion" (Allison and Ghormley [11]). The fact that the bones from the denervated legs without marked alterations in the hip joints show no other changes suggests that the increase in weight in the femurs and tibias of the denervated limbs is a functional response to the altered conditions in the hip joints. This increase in weight may be a compensatory reaction to the destruction of the cartilage on the head of the femur, or it and the arthritic changes may have resulted from the use of the limb in an abnormal position. This supposition is supported by the occurrence of changes in the hip joints only in the deafferented limbs of animals which had considerable freedom.

Wright and Pemberton [12] found that 75 per cent of arthritic subjects have a lower peripheral surface temperature than normal persons under comparable circumstances. Hinsey [13] found a marked lowering of skin temperature in the deafferented limbs of cats. Just why section of the posterior roots should cause such a fall in skin temperature is not known, but several possibilities suggest themselves. If the dorsal roots contain vasodilator fibers, these would be interrupted, and their loss would probably result in a decreased peripheral skin temperature

10. Knaggs, R. L.: The Inflammatory and Toxic Diseases of Bone, Bristol, John Wright & Sons, Ltd., 1926.

11. Allison, N., and Ghormley, R. K.: Diagnosis in Joint Disease, New York, William Wood & Company, 1931.

12. Wright, L., and Pemberton, R.: The Peripheral Surface Temperature in Arthritis, Arch. Int. Med. **45**:147 (Jan.) 1930.

13. Hinsey, J. C.: Observations on Skin Temperatures in Hind Limbs Deprived of Their Sensory and Sympathetic Nerve Supply, Am. J. Physiol. **109**: 53, 1934.

Another possibility is that the afferent fibers from the skin exert an inhibiting effect on the preganglionic vasoconstrictor sympathetic fibers and that interruption of the sensory pathway leads to an overactivity of the vasoconstrictor fibers. It is possible that the reduced peripheral skin temperature found in arthritic patients is the result of a decreased sensory supply to the limbs. Pearson [14] and Newman and Corbin [14a] reported a striking decrease in vibratory sensibility of the lower extremities in persons after the fifth decade of life. Hypertrophic arthritis is known to be a disease seen most commonly in the later decades of life. Whether a patient with this condition has a more reduced peripheral sensibility than an unaffected person of the same age, I am not ready to assert, but work in progress suggests that this may be the case (Newman and Corbin).

A statement from the report of the Second Conference on Rheumatic Diseases of the Mayo Clinic (Hench [15]) is likewise somewhat suggestive in this respect, for it is there stated: "No explanation was given as to why many badly worn joints, with extensive hypertrophic arthritis, are painless, whereas other joints only slightly altered are so painful that locomotion is difficult. Only about 7 per cent of Keefer's patients suffered pains in the joints." Eloesser [9] also stressed the importance of anesthesia and consequent trauma in the development of Charcot-like joints in the deafferented limbs of cats.

Ellis [16] found a steady decrease in the number of Purkinje cells in man with advancing age, and Inukai [17] made the same observation in rats. Duncan [18] found a 10 per cent decrease in the number of ventral root fibers in old rats. He also found a small number of fibers exhibiting wallerian degeneration in the peripheral nerves of animals of all ages. This would tend to show that a continual slight degeneration of nerve fibers occurs throughout life. Recently Corbin and Gardner [19] have found a diminution in the number of spinal root myelinated fibers in the senile human subject.

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14. Pearson, G. J.: Effect of Age on Vibratory Sensibility, Arch. Neurol. & Psychiat. **20**:482 (Sept.) 1928.

14a. Newman, H. W., and Corbin, K. B.: Quantitative Determination of Vibratory Sensibility, Proc. Soc. Exper. Biol. & Med. **35**:273 (Nov.) 1937.

15. Hench, P. S.: Report on Second Conference on Rheumatic Diseases, Proc. Staff Meet., Mayo Clin. **8**:573 (Sept. 20) 1933.

16. Ellis, R.: Norms for Some Structural Changes in the Human Cerebellum from Birth to Old Age, J. Comp. Neurol. **32**:1, 1920.

17. Inukai, T.: On the Loss of Purkinje Cells, with Advancing Age, from the Cerebellar Cortex of the Albino Rat, J. Comp. Neurol. **45**:1, 1928.

18. Duncan, D.: A Determination of the Number of Nerve Fibers in the Eighth Thoracic and the Largest Lumbar Ventral Roots of the Albino Rat, J. Comp. Neurol. **59**:47, 1934.

19. Corbin, K. B., and Gardner, E. D.: Decrease in Number of Myelinated Fibers in Human Spinal Roots with Age, Anat. Rec. **68**:63 (April 25) 1937.

Eloesser's work showed that deafferentation alone, without concomitant sympathectomy, suffices to produce Charcot-like joints. Tabetic arthropathy is a clinical condition in which the only known causative local factor is anesthesia, but how diminished sensibility of a joint can produce a "deforming arthritis" is not known. A number of ancillary factors, such as senility and arteriosclerosis, undoubtedly contribute to its pathogenesis in man, but with diminished sensibility, the proprioceptive mechanism, which ordinarily protects against malposition and motion beyond the normal range, is impaired, so that areas of the articular surfaces, ligaments and capsules, unadapted for the stresses to which they are subjected, may be traumatized. If there also is a diminished blood supply as the result of senile arteriosclerosis and of the vasoconstriction, which may accompany reduced sensibility, the hyaline articular cartilage may suffer nutritional disturbances and become more susceptible to traumatic injuries. As soon as destruction of the cartilage has begun, the initial wear is intensified through the increased friction between less resistant and roughened surfaces. These, to be sure, are merely suggestions, and I realize that the question will have to be studied from many other aspects before a definite decision can be reached.

Dr. J. C. Hinsey furnished the material for this study.

MALIGNANT TUMORS OF MECKEL'S DIVERTICULUM

REPORT OF A CASE OF LEIOMYOSARCOMA

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AND
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A malignant tumor of Meckel's diverticulum is rare enough to be considered a pathologic curiosity. The literature on other lesions associated with Meckel's diverticulum, however, is increasing each year. We have therefore thought it opportune to combine the report of a case of a malignant tumor of Meckel's diverticulum with a general survey of the literature.

Meckel's diverticulum is a developmental anomaly of the intestinal tract which is found in about 2 per cent of all adults. The mechanism responsible for the production of this anomaly, as is well known, is failure of the omphalomesenteric duct and its accompanying vessels to become completely obliterated. Normally this obliteration takes place in the third to the fifth week of embryonic life. The yolk stalk may fail to become completely obliterated, leading in rare cases to an intestinal fistula opening through the umbilicus; occasionally the duct becomes obliterated, except at its distal part. In the latter instance an umbilical fistula is formed with secretion from still active glandular elements in the mucosa of the open duct. Occasionally these cells may undergo hyperplastic changes and form a neoplasm of the umbilicus. In other instances the proximal and distal parts of the omphalomesenteric duct may be closed, but an opening may remain in the middle part of the duct. As a result of the secreting activity of the remaining cells of the duct, a retention cyst may be formed, a so-called enterocystoma. In case only the proximal part of the omphalomesenteric duct is closed, a true Meckel's diverticulum is formed. It appears, however, that any of these various types of developmental anomalies may be combined (fig. 1).

True Meckel's diverticulum is usually located in the ileum about 100 cm. from the ileocecal valve; in rare cases, however, it may be found anywhere in the gastro-intestinal tract from the cardia to the

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rectum. Such diverticula vary greatly in size, but they usually reach from 2.5 to 10 cm. in length and are most frequently found on the antimesenteric border. With these variations in mind, it will be readily understood that the location and the gross appearance may not be sufficient evidence on which to base a diagnosis of true Meckel's diverticulum. Attempts have been made by microscopic examination to lay down definite requirements for the diagnosis of such a diverticulum.

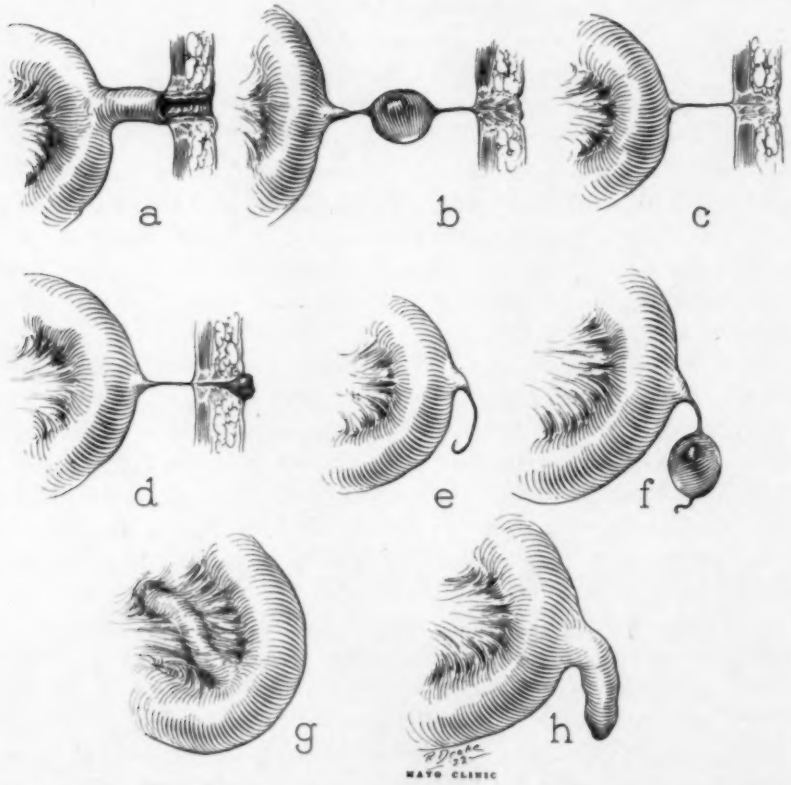

Fig. 1.—Various types of developmental anomalies: *a*, patent duct opening onto the abdominal wall at the umbilicus; *b*, the duct occluded at its end so that a cyst is formed somewhere in its length; *c*, the duct obliterated but remaining attached to the umbilicus; *d*, the duct remaining attached to the umbilicus and with intestinal mucosa at its outer end; *e*, the duct obliterated and hanging with a free end within the abdominal cavity; *f*, the duct hanging within the abdominal cavity and forming a cyst; *g*, the duct lying within the mesentery of the small intestine, and *h*, the duct remaining as a small patent projection from the ileum. (This illustration was redrawn from Dixon and Steward.[4a])

These attempts, however, have proved only partly successful because of the somewhat inconsistent histologic characteristics of the mucosa of the diverticulum.

Farr and Penke,[1] in a review of the surgical files of the New York Hospital, found gastric mucosa reported in 6 of 13 Meckel's diverticula. According to Schaetz,[2] 57 per cent of 30 Meckel's diverticula that were examined carefully contained only normal ileac mucosa. In the remaining 13 diverticula in his series, jejunal mucosa was found in 3, gastric mucosa in 5, pancreatic tissue in 3, carcinoid tissue in 1 and peritoneal epithelium in 1.

As has been said, Meckel's diverticulum is only a developmental anomaly, and no doubt many people have gone through life without ever having had any symptoms from it. Studies of the records of 2,050 necropsies at the New York Hospital from 1916 to 1931 revealed Meckel's diverticulum as an incidental finding in 13 cases; it had given rise to intestinal strangulation in only 1 instance.

Meckel's diverticulum appears to be found more frequently in males than in females, the incidence according to Christie [3] being 75 per cent in males as compared to 25 per cent in females, with an incidence of approximately 1.1 per cent in all persons.

It appears from the increased number of reports on the subject in last year's medical literature that Meckel's diverticulum is potentially the source of many different pathologic conditions, diverticula having been reported to have given rise to pathologic changes in from 25 to 33 per cent of cases. The pathologic changes associated with Meckel's diverticulum are given in the following outline. No doubt with greater experience this outline will prove to be incomplete. It is presented here in the hope that it may facilitate a survey of the various pathologic potentialities of Meckel's diverticulum.

Pathologic Conditions Associated with Meckel's Diverticulum

A. Mechanical disturbances:

1. Gangrene of the diverticulum after strangulation or excessive rotation of a long diverticulum
2. Intestinal ileus following eversion of part of the intestine into the diverticulum or invagination of the diverticulum into the intestines, strangulation of the intestine by the diverticulum or its band formations or kink formations by pulling of bands and adhesions.
3. Disturbances caused by a hernial sac containing a diverticulum
4. Disturbances arising when a diverticulum is associated with the developmental anomaly of congenital ileac atresia and ileac stenosis

1. Farr, C. E., and Penke, Madeline: Meckel's Diverticulum, Ann. Surg. **101**:1026-1041 (April) 1935.

2. Schaetz, Georg: Beiträge zur Morphologie des Meckel'schen Divertikels (Ortsfremde Epithelformationen im Meckel), Beitr. z. path. Anat. u. z. allg. Path. **74**:115-224, 1925.

3. Christie, A. U., cited by Michael and Bell.[14]

B. Inflammatory disturbances, varying from mild catarrhal inflammation to gangrene, with perforation and peritonitis (diverticulitis):

1. Nonspecific inflammation, caused by:
   (*a*) Trauma
   (*b*) Foreign bodies (calculi)
   (*c*) Parasites
   (*d*) Idiopathic diverticulitis
2. Specific inflammation, caused by:
   (*a*) Tuberculosis
   (*b*) Typhoid

C. Heterotopic tissue formations:

1. Accessory pancreatic tissue
2. Normal, hypertrophic or ulcerating mucosa from the gastro-intestinal tract, leading to diverticulitis, with or without ulceration and subsequent intestinal hemorrhage

D. Neoplastic disease (exclusive of enterocystoma):

1. Benign tumor:
   (*a*) Myoma
   (*b*) Lipoma
   (*c*) Carcinoid tumor
   (*d*) Neuroma
   (*e*) Papilloma
2. Malignant tumor:
   (*a*) Carcinoma
   (*b*) Sarcoma

So-called heterotopic tissue formations in Meckel's diverticulum have for many years attracted the interest of embryologists, histologists and pathologists. Most frequently such tissue consists of aberrant pancreatic tissue, gastric mucosa or mucosa from other portions of the intestinal tract. These various tissue formations may be present alone, or they may be mixed, and they may or may not appear grossly as a tumor. A most extensive and interesting investigation of heterotopic tissue formations was made by Schaetz. The clinical importance of these particular anomalies is emphasized by the occasional finding of ulcerations and subsequent hemorrhage in heterotopic tissues.[4]

In connection with benign tumors of Meckel's diverticulum it may be mentioned that a myoma giving rise to ileus was removed from a

4. (*a*) Dixon, C. F., and Steward, J. A.: Diverticulum with Hemorrhage: Omphaloadenoma, S. Clin. North America **12**:1025-1031 (Aug.) 1932. (*b*) Schullinger, R. N., and Stout, A. P.: Meckel's Diverticulum: Report of a Case of Hemorrhage in the Bowel Associated with a Meckel's Diverticulum that Presented an Adenoma Composed of Gastric and Duodenal Glands, Arch. Surg. **28**: 440-466 (March) 1934.

9 year old boy by Höpfner.[5] A lipoma in the same location was described by Macé de Lépignay.[6] Of greater importance than these, however, are the so-called carcinoid tumors.

Oberndorfer[7] in 1907 reviewed a few cases of tumor of the small intestine in which the growths had the same microscopic picture as carcinoma but differed in several other respects, enough so to warrant separation of this type of tumor from the malignant tumors and classification of it under the "carcinoid tumors." Lubarsch[8] and others had earlier called attention to this group of tumors. In the same paper Oberndorfer described finding a carcinoid tumor of Meckel's diverticulum in a man 68 years of age who had died of cerebral arteriosclerosis. Later, similar reports appeared in the literature. Schaetz in 1925, in a study of 30 cases of Meckel's diverticulum, found small groups of epithelial cells in the tip of the diverticulum in a 69 year old man who had died of bronchopneumonia. These cells had the characteristics of those found in carcinoid tumor. Stewart and Taylor[9] reported finding a typical carcinoid tumor the size of a pea in a diverticulum removed at postmortem examination from a man 54 years old who had died of coronary sclerosis. Finally, Price[10] in 1935 removed an inflamed and obstructed Meckel's diverticulum from a woman 54 years of age who had had generalized abdominal pain and signs of peritonitis for one day. On microscopic examination the diverticulum was found to contain a carcinoid tumor.

Hicks and Kadinsky[11] reported a case of carcinoid tumor in 1922, but Stewart and Taylor, who had occasion to examine the slides, were of the opinion that the lesion was not a carcinoid tumor but heterotopia of the gastric mucosa.

CARCINOMA OF MECKEL'S DIVERTICULUM

The following are abstracts of cases of carcinoma of Meckel's diverticulum reported in the literature.

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5. Höpfner, E.: Ein eigenartiger Fall von Divertikel-Ileus, Arch. f. klin. Chir. **97**:1058-1073 (April 4) 1912.

6. de Lépignay, Macé, cited by Hässner.[23]

7. Oberndorfer, Siegfried: Karzinoide Tumoren des Dünndarms, Frankfurt. Ztschr. f. Path. **1**:426-432, 1907.

8. Lubarsch, cited by Franke.[15]

9. Stewart, M. J., and Taylor, A. L.: Carcinoid Tumour of Meckel's Diverticulum, J. Path. & Bact. **29**:135-136, 1926.

10. Price, I.: Carcinoid Tumour of a Meckel's Diverticulum: Report of a Case, Brit. J. Surg. **23**:30-34 (July) 1935.

11. Hicks, J. A. B., and Kadinsky, S.: A Case of "Carcinoid Tumour" of Meckel's Diverticulum, Lancet **2**:70 (July 8) 1922.

Wiseley [12] in 1931 reported intestinal resection for medullary carcinoma of Meckel's diverticulum located about 76 cm. from the ileocecal valve in a man 41 years of age.

In the laboratory of surgical pathology at the Johns Hopkins Hospital, 11 instances of Meckel's diverticulum were encountered among 50,000 pathologic specimens. According to Copeland,[13] 1 of these diverticula was the seat of an adenocarcinoma involving the umbilicus, and it had grown to such an extent that the exact relations of the ileum, the diverticulum and the umbilicus were rather indistinct.

Michael and Bell [14] in 1932 described an adenocarcinoma of Meckel's diverticulum removed at operation from a man 76 years of age.

Franke [15] in 1933 described a necrotic adenocarcinoma of Meckel's diverticulum removed at operation from a 54 year old man.

Rexwald Brown [16] in 1933 described a degenerating medullary carcinoma, probably of Meckel's diverticulum, removed at operation from a man 62 years of age. The tumor was about the size and shape of a cauliflower and had given rise to general peritonitis.

Gray and Kernohan [17] reported an intestinal resection of part of the ileum for tumor of a diverticulum that had doubly invaginated the ileum. The patient was a woman 37 years of age. The tumor was the size of a walnut and was made up of two well differentiated parts, the proximal part consisting of heterotopic gastric mucosa and the distal part of adenocarcinomatous tissue of grade 2. The main clinical symptom was vague abdominal distress. Bimanual palpation revealed a slightly tender mass in the ileocecal region, but the peculiar thing about this palpatory finding was that one day the tumor could be easily felt, whereas on other days it was difficult or even impossible to feel it at all.

SARCOMA OF MECKEL'S DIVERTICULUM

While sarcoma of the small intestine is comparatively rare, it appears that a slightly greater number of sarcomas of the small intestine have been reported than of carcinomas in that region. In 569 cases of carcinoma Lubarsch [8] found only 0.3 per cent of carcinomas of the

12. Wiseley, A. N.: Medullary Carcinoma of Meckel's Diverticulum, J. A. M. A. **96**:1949-1950 (June 6) 1931.

13. Copeland, cited by Wiseley.[12]

14. Michael, Paul, and Bell, H. G.: Primary Adenocarcinoma Arising in a Meckel's Diverticulum, Surg., Gynec. & Obst. **54**:95-97 (Jan.) 1932.

15. Franke, Kurt: Ueber ein primäres Carcinom in einem Meckelschen Divertikel, Ztschr. f. Krebsforsch. **39**:206-216 (April) 1933.

16. Brown, Rexwald: Carcinoma of Meckel's Diverticulum, S. Clin. North America **13**:1283 (Dec.) 1933.

17. Gray, H. K., and Kernohan, J. W.: Unpublished data.

ileum. Magnusson [18] collected reports of 98 cases of sarcoma of the small intestine from the literature in 1934. In this series there appeared to be an equal incidence of sarcoma of the ileum and sarcoma of the jejunum, a preponderance of males being affected. In the 91 cases in which the sex was stated, 61 of the patients were males and 30 were females, their ages varying from 5 days to 81 years. Magnusson did not state, however, how many cases of sarcoma of Meckel's diverticulum were included in this series.

In a review of the literature we have been able to find reports of 12 cases of sarcoma of Meckel's diverticulum. In addition to this, there are 2 unpublished cases from the Mayo Clinic. It appears, therefore, that sarcomas of Meckel's diverticulum do not account for more than from 12 to 14 per cent of all sarcomas of the small intestine. The following are abstracts of cases of sarcoma of Meckel's diverticulum which were reported:

The first report of a case of sarcoma of Meckel's diverticulum was made by Virchow, who, according to Fried,[19] described the tumor in a new-born infant. It was a spindle cell sarcoma that pressed out through the umbilical ring. The sex of the infant was not given.

Kaufmann [20] in 1890 described a case of myxosarcoma telangiectodes.

Fried [19] in 1902 described a myosarcomatous tumor the size of two fists which was found at postmortem examination on a man 55 years of age. The tumor was located about 120 cm. above the ileocecal valve, and there was metastasis to the regional lymph nodes and to the liver. The clinical diagnosis in this case was acute peritonitis (intestinal embolus).

The Basler [21] collection contains the report of a case in which a spindle cell sarcoma of Meckel's diverticulum the size of a hen's egg was found in a woman 72 years of age.

Tschiknawerow [22] found a spindle cell sarcoma of Meckel's diverticulum during postmortem examination on a woman 62 years of age, who had died from fibrinopurulent acute peritonitis following torsion of the ileum, with necrosis and perforation of the diverticulum.

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18. Magnusson, Ragnar: Sarcoma of Small Intestine, in Connection with a Case of Haemangiosarcoma of the Jejunum, Acta chir. Scandinav. **73**:576-590, 1934.

19. Fried, cited by Franke.[15]

20. Kaufmann, cited by Franke.[15]

21. Basler, cited by Kaufmann, Eduard: Lehrbuch der speziellen pathologischen Anatomie für Studierende und Aerzte, Berlin, W. de Gruyter & Co., 1922, vol. 1, p. 571.

22. Tschiknawerow, Leon: Zur Kenntnis der pathologischen Gewebsbildungen im Meckel'schen Divertikel, Berl. klin. Wchnschr. **48**:1676-1679 (Sept. 11) 1911.

Hässner [23] found at necropsy a degenerating sarcoma of Meckel's diverticulum in a man 50 years of age who had been operated on after a few days' illness for beginning peritonitis. He had died two days after the operation.

Symmers [24] reported finding a leiomyosarcoma of Meckel's diverticulum in a man aged 22. The lesion was discovered incidentally during an operation for hernia and was situated 30 cm. above the ileocecal valve. No clinical symptoms were associated with it.

Black [25] reported removal of a huge tumor weighing 2,460 Gm. from a woman 59 years of age. The tumor was a papillomatous cystadenoma of potentially malignant type and was thought to have originated in a diverticulum (either acquired or congenital) in the sigmoid colon.

Crile and Portmann [26] reported a case in which a spindle cell sarcoma of Meckel's diverticulum was removed from a woman 41 years of age; the tumor was the size of a pear. At the time of the physical examination a small mass was palpated in the right lower abdominal quadrant.

Mathews [27] in 1925 removed a myoma from the ileum of a man 44 years of age. The patient was referred to him because of a large abdominal mass reaching from the culdesac to about the level of the umbilicus. During examination the tumor had suddenly lost its tenseness simultaneously with the onset of severe abdominal pain, for which reason emergency laparotomy was performed after a lapse of two hours. The patient recovered and felt fine for about four and a half years, when the hypogastric tumor recurred. It was removed after a few months. At the second examination there were palpatory signs of recurrence. The tumor removed at the second operation was a leiomyosarcoma, a finding which makes it reasonable to assume that the tumor may have had sarcomatous characteristics at the time of the first operation.

According to Oberndorfer, there are all stages of transition from myoma to myosarcoma, a peculiarity which is the basis of one of the greatest controversies regarding tumors of the intestinal tract.

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23. Hässner, Hugo: Zur Pathologie des Meckelschen Divertikels (Fall von Sarkom des Meckelschen Divertikels), Frankfurt. Ztschr. f. Path. **14**:501-516, 1913.

24. Symmers, Douglas: The Association of Malignant Myomata with Meckel's Diverticulum, Ann. Surg. **70**:183-187 (Aug.) 1919.

25. Black, W. T.: Congenital Diverticula of the Intestines: Report of a Case of a Tumor Growing from the Tip of an Apparently Congenital Diverticulum in the Lower Sigmoid Region, Surg., Gynec. & Obst. **28**:473-477 (May) 1919.

26. Crile, G. W., and Portmann, U. V.: A Primary Spindle Cell Sarcoma of Meckel's Diverticulum, Surg., Gynec. & Obst. **41**:615-617 (Nov.) 1925.

27. Mathews, F. S.: Meckel's Diverticulum: A Report of Twelve Cases, Including One Tumor, Arch. Surg. **10**:720-729 (March) 1925.

König [28] in 1930 demonstrated a spindle cell sarcoma the size of a fist in a diverticulum. It led to fatal peritonitis due to necrosis of the tumor and perforation into the abdominal cavity.

Faust and Walters [29] in 1931 reported the removal of a diverticulum containing a fibrosarcoma from a man 62 years of age. The outstanding symptom in this case was intestinal hemorrhage leading to secondary anemia. The patient reentered the clinic in February 1936, that is, a little less than six years after removal of the intestinal tumor. Six months previously he had accidentally discovered a mass in the right lower abdominal quadrant, and this had gradually increased in size, causing distention and constipation of increasing severity. No

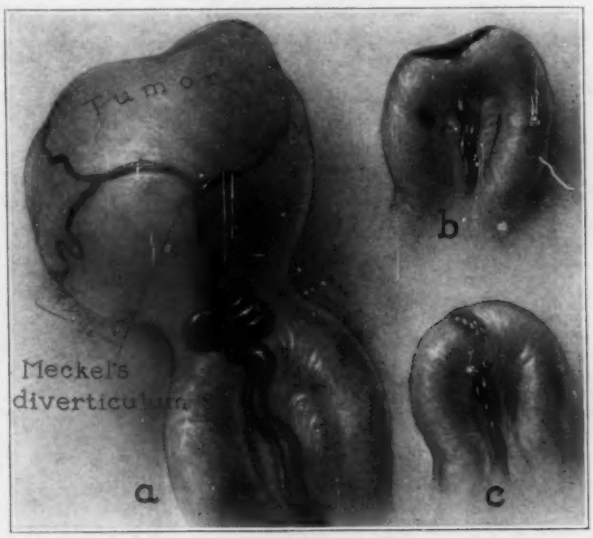

Fig. 2.—Part of the ileum with Meckel's diverticulum, shown in *a*. The blood vessels from the mesentery extend up to the tumor. In *b*, the blood vessels have been ligated and the diverticulum and the tumor excised, and in *c*, the opening in the ileum has been transversely sutured.

recurrence of the gastro-intestinal hemorrhage was noted at the time of the second examination. There was moderate secondary anemia, the value for hemoglobin amounting to 9.7 Gm. per hundred cubic centimeters and the erythrocytes numbering 4,500,000 per cubic milli-

28. König, E.: Sitzungsberichte aus chirurgischen Gesellschaften: XXXIX. Tagung der Vereinigung nordwestdeutscher Chirurgen am Freitag, dem 13. und Sonnabend, dem 14. Dezember 1929 im Allgemeinen Krankenhause Barmbeck in Hamburg. (Offizieller Bericht), Zentralbl. f. Chir. **57**:1107 (May 3) 1930.

29. Faust, L. S., and Walters, Waltman: Fibrosarcoma of a Meckel's Diverticulum Producing Intestinal Hemorrhage, Minnesota Med. **14**:233-236 (March) 1931.

meter of blood. A large mass was found that filled most of the right side of the abdomen and extended into the right flank. The most probable diagnosis was recurrence of the fibrosarcoma of the small intestine. Because of the size of the tumor and the poor general condition of the patient, exploratory laparotomy was not deemed advisable, and roentgen therapy was employed.

Kernohan,[30] in reviewing the records of approximately 140 cases in which a diverticulum was removed at operation or at necropsy at the Mayo Clinic, found 1 in which a leiomyosarcoma of Meckel's diverticulum had been removed from a 66 year old woman by Dr. Judd in 1926.[31] At operation 1 inch (2.5 cm.) of the ileum was excised, and a calcareous Meckel's diverticulum lying behind the uterus

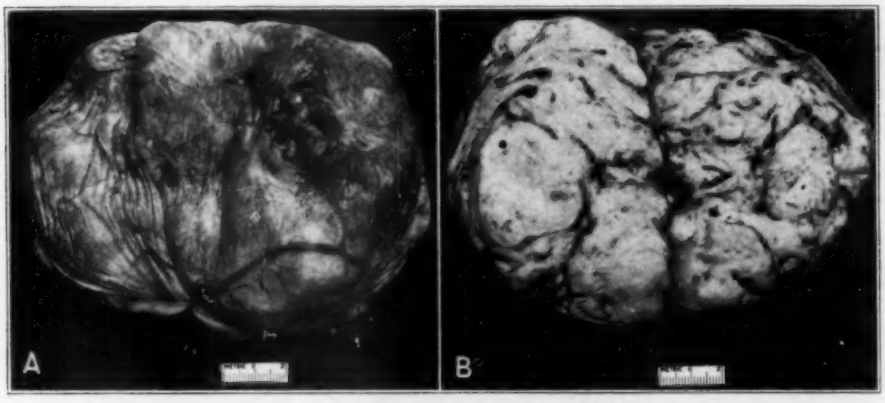

Fig. 3.—*A*, the diverticulum and tumor removed at operation. *B*, the specimen of the diverticulum and tumor cut open.

was removed. The diverticulum contained a tumor the size of a grapefruit, which on microscopic examination proved to be a myosarcoma, grade 2, with a neuroma.

REPORT OF A CASE OF LEIOMYOSARCOMA OF MECKEL'S DIVERTICULUM

A man aged 62 registered at the clinic in January 1936. In the previous seven years he had been bothered with episodes of epigastric fullness followed by nausea, which were relieved by induced vomiting; these attacks were never associated with any real pain. On examination the patient did not appear to be sick. Palpation of the abdomen did not reveal any distention or tenderness or any masses. Bimanual rectal palpation, however, revealed a tumor in the culdesac anterior to the rectum; it measured about 5 by 7 cm., was movable and rather hard and had a smooth surface. It was not tender to pressure and appeared to be distinctly

30. Kernohan, J. W.: Personal communication to the authors.

31. This case will be reported subsequently.

separate from the prostate gland and seminal vesicles. The palpatory findings, however, seemed to change from day to day. Proctoscopic examination proved the tumor to be extrinsic to the rectum and the lower part of the sigmoid colon. An enema of barium sulfate indicated a normal colon and terminal portion of the ileum. Examination otherwise gave negative results, except for the finding of a small duodenal ulcer on roentgenographic examination of the stomach. Abdominal exploration, performed on January 14, revealed an encapsulated tumor of the ileum, about 10 cm. in diameter, completely filling a diverticulum. One large vein 5 mm. in diameter and an artery half that size extended up from the mesentery of the ileum in a tortuous fashion over the side wall of the ileum and up into the tumor (fig. 2). These vessels were divided and ligated, after which the tumor was excised from the ileum with a cutting cautery; the opening in the ileum was closed transversely.

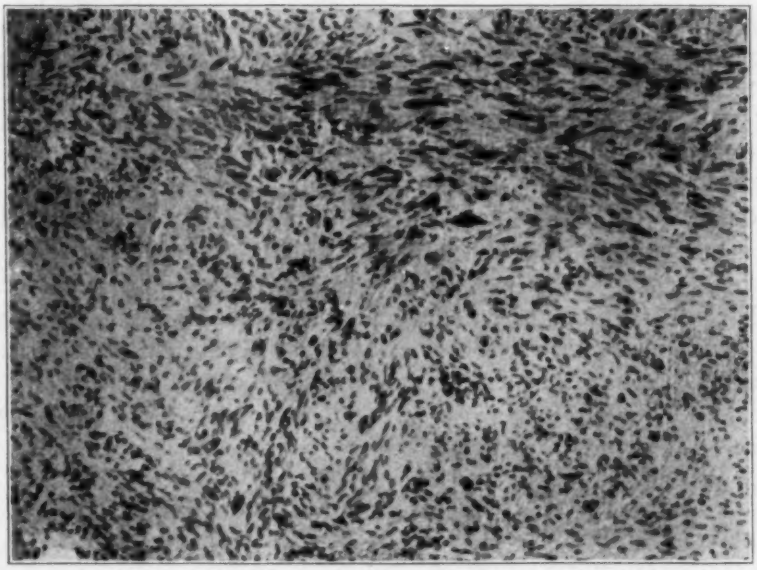

Fig. 4.—Section of the tumor, showing well differentiated bundles of smooth muscle tissue in a fibrous stroma. In some places the tumor cells are more clearly packed and more ovoid and hyperchromatic, an occasional mitotic figure being present. The diagnosis was leiomyosarcoma of a low grade of malignancy.

The postoperative course was uneventful. The tumor was pedunculated and ovoid and was firm and rubbery in consistency (fig. 3). It was situated in the submucosa on intramuscular layers of intestinal wall and was well encapsulated without producing any ulceration of the mucosa. Grossly, the tumor appeared to be composed of large whorls of myomatous tissue similar to that of leiomyoma of the uterus. Microscopically, it was found to be composed of well differentiated bundles of smooth muscle in tumor formation lying in a fibrous stroma. In some areas the tumor cells were more closely packed and more ovoid and hyperchromatic, and there was an occasional mitotic figure. The pathologic diagnosis was leiomyosarcoma of a low grade of malignancy (fig. 4).

COMMENT

In the survey that we have made we have found a total of 20 cases of malignant tumors of Meckel's diverticulum: 6 cases of carcinoma and 14 of sarcoma. In the 16 cases in which the sex was stated, 8 of the patients were males and 8 were females. In view of the statement that Meckel's diverticulum is found three times more frequently in males than in females, it would appear from this compilation that there may be a greater tendency toward a malignant growth in Meckel's diverticulum in females than in males. However, this finding may be entirely changed by analysis of a larger series of cases.

One of the cases of carcinoma reviewed in this series (the one reported by Gray and Kernohan) is of particular interest to pathologists. In this case an adenocarcinoma was found growing in a tumor formed of heterotopic gastric mucosa. If the patient had continued to live without an operation, it would, according to the authors, have been only a question of time before the carcinoma had infiltrated the entire heterotopic gastric mucosa and left no trace of its origin in this tissue.

One wonders whether in other cases reviewed in this series carcinoma of Meckel's diverticulum may not have originally begun in heterotopic gastric tissue, further growth of the tumor possibly having made further differentiation of tissue structures impossible. This raises the question whether carcinoma of Meckel's diverticulum may be considered from the same point of view as gastric carcinoma. An accurate account of the percentage of various heterotopic tissues in a large series of Meckel's diverticula would be of importance in this connection. Schaetz, who examined 30 cases, found heterotopic tissue formation in 43 per cent, in 38.5 per cent of which the tissue consisted of gastric mucosa.

If this series of 6 cases of carcinoma and 14 cases of sarcoma of Meckel's diverticulum is again considered, the prevalence of sarcoma so far seems obvious. Considering malignant tumors of the stomach, the relation is exactly the reverse, gastric sarcomas making up about 1 per cent of all malignant gastric tumors. It seems only reasonable, therefore, to conclude that in considering the formation of malignant tumors of Meckel's diverticulum the condition is in no way explained by the types of heterotopic tissues found. In other words, there does not seem to be any exact parallelism between pathologic processes in Meckel's diverticulum and pathologic processes in organs from which the heterotopic tissue of a diverticulum may be considered to have been derived. Still it appears that the heterotopic tissue undoubtedly plays an important rôle in the pathologic process in the organ under discussion.

With the small series of malignant tumors at hand it seems impossible to try to bring out the suggestive symptoms in these cases. In a review of the available clinical data in this series, there are, however, certain points which may be emphasized: A malignant tumor of Meckel's diverticulum may be present without, for a time at least, producing any clinical symptoms, as in the case described by Symmers. When clinical symptoms were associated with malignant tumor of Meckel's diverticulum, the symptoms recorded appeared naturally to fall into two main groups: (1) primary symptoms referable to the presence of the tumor and (2) secondary symptoms referable to the perforation of the diverticulum, leading to localized or diffuse peritonitis or to invagination of the tumor together with the diverticulum.

Unfortunately, in this series the primary symptoms which may reasonably be assumed to be caused by the tumor itself were rather vague. In order to simplify the matter, they may be considered under the following two subheadings: 1. Symptoms of abdominal distress or pain. Abdominal distress appears to have occurred in more than 50 per cent of the cases; it was of an intermittent colicky type and of a moderate degree and was usually located in the right side of the lower part of the abdomen, with frequent projection to the epigastrium. 2. Symptoms caused by the presence of an abdominal tumor. In 5 cases a palpatory finding of a tumor had been made prior to operation. In 2 of these cases the growth presented itself as a pelvic tumor, and in only 2 was it found in the ileocecal region. A palpatory finding which may be of some consequence in localizing the tumor is the occasional tendency for the growth to escape partly or completely from the palpating hand, a phenomenon which suggests the presence of a tumor in the ileum. Regarding secondary symptoms referable to intestinal invagination and ileus, Harkins,[32] after reviewing the literature dealing with intestinal intussusception, concluded that Meckel's diverticulum is a factor in causing intussusception in only 2.5 per cent or less of cases. Considering the great number of Meckel's diverticula reported as compared to the 20 cases of malignant tumors of Meckel's diverticulum reviewed here, one will realize the remote chance of encountering a malignant tumor in a diverticulum that gives rise to intussusception. In this series, in only 1 case (that of Gray and Kernohan) did a malignant tumor lead to intussusception.

Symptoms of localized or diffuse peritonitis were encountered in 4 cases in this series. In 3 of them the diffuse peritonitis resulted from necrosis and perforation of the diverticulum, and the patients died:

32. Harkins, H. N.: Intussusception Due to Invaginated Meckel's Diverticulum: Report of Two Cases with a Study of One Hundred and Sixty Cases Collected from the Literature, Ann. Surg. **98**:1070-1095 (Dec.) 1933.

in the fourth case local peritonitis arising from a ruptured appendix was diagnosed preoperatively, and the patient recovered after the operation.

In considering the foregoing symptoms, one is left with the impression that they are of little direct diagnostic importance and that they may also fit a variety of abdominal conditions to be considered at the bedside. The condition under discussion, however, is primarily a surgical problem, and the surgeon may be interested in knowing how great a chance he has of getting the patient to operation even when no clinical diagnosis has been made preoperatively. There is good reason to expect that all patients presenting an abdominal tumor or clinical signs of intussusception and ileus or peritonitis will be considered as needing surgical assistance. On this basis, 9 of the patients in this series would be considered candidates for surgical exploration. In other words, we have reason to expect that at least 50 per cent of patients with malignant tumors of Meckel's diverticulum would be referred for surgical treatment.

In the cases reviewed no evidence of metastasis was ever found. In 2 cases, however (1 of Mathews and 1 of Faust and Walters), there was evidence of recurrence of the tumor, in both cases five years after its removal. This, of necessity, makes for a guarded prognosis.

OLFACTOMETRY IN CASES OF ACUTE HEAD INJURY

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NEW YORK

A new quantitative method of testing the sense of smell has recently been described.[1] Whereas by all former methods odors were carried to the olfactory membrane through inhalation or sniffing, by this new method the odorous substance is injected by a process called "blast injection" into one or both nasal passages during cessation of breathing. The known force of the injection takes the place of the inspiratory movement. In this test the volume of air and odor and the pressure of the injection can be measured. "By this test it has become possible to study the threshold of olfactory sensibility, to determine fixed values (olfactory coefficients) for each odor and to gain considerable information regarding the relative importance of the volume and pressure of the olfactory stimulus." [2]

The originators of this method have made practical use of it in the localization of supratentorial tumors of the brain. They have found diminution in unilateral or bilateral olfactory acuity and prolongation of olfactory fatigue dependent on the location of the tumor. These responses appear to be so characteristic that from them alone the position of a tumor interfering with the olfactory mechanism may often be determined.

It was considered advisable to apply this method of olfactometry to the acute traumatic craniocerebral encephalopathies in order to determine the frequency and nature of olfactory disturbances in such injuries. The patients used for the study were found in the skull fracture division of the traumatic surgical service of the Harlem Hospital.

From the Surgical Service of Dr. Louis T. Wright, Harlem Hospital, Dr. Charles S. Cassasa, Director.

1. Elsberg, C. A., and Levy, I.: The Sense of Smell: A New and Simple Method of Quantitative Olfactometry, Bull. Neurol. Inst. New York **4**:5 (March) 1935.

2. Elsberg, C. A.; Brewer, E. D., and Levy, I.: The Sense of Smell: The Relative Importance of Volume and Pressure of the Impulse for the Sensation of Smell and the Nature of the Olfactory Process, Bull. Neurol. Inst. New York **4**: 264 (Oct.) 1935.

The following form was drawn up to simplify the recording of data:

1. Location of fracture and type (if present).....
2. Area of contusion or laceration of the scalp.....
3. Orifice of bleeding .....
   (Presence or absence of spinal fluid)
4. Localizing neurologic signs.....
5. Probable areas of damage to the brain.....

	Left	Right	Direct	Contrecoup
Frontal				
Temporal				
Parietal				
Occipital				

6. Red blood cells in the spinal fluid.....
7. Remarks:
   (*a*) Conscious on admission
   (*b*) Unconscious on admission

The only persons who were considered for study were those who showed no nasal or oral bleeding. (A number of patients were tested by means of the blast injection test in whom it was felt that bleeding had come from about the roof of the nasal cavities. In many instances the olfactory coefficients were elevated. If such bleeding was unilateral, the high olfactory coefficient [3] was usually apparent on this side). The initial test was made when the patient was well enough to sit up in bed and when the sensorium had cleared. A definite procedure was established for all patients for the blast injection test. Before each injection the patient was told to take a deep breath, then to raise the hand as a signal that the breath was being held. After the injection he was instructed to release his breath through the nose. After the blast had been released into the nostril, a short period of time was allowed to elapse before the nose pieces were taken away. In this way there was no confusion whether there was perception of the odor immediately on release of the blast injection or after the expiration when some particles of odor trapped in the nasal cavities might impinge on the olfactory mucous membrane.

It was felt that anterior rhinoscopy was essential in each case before olfactometry was done. Various local conditions of the nose, such as colds and polypi, can produce various degrees of respiratory anosmia. One patient who was sent to the hospital for olfactometry after an intracranial injury complained of anosmia, the onset of which he traced

3. The smallest number of cubic centimeters of an odor that can be identified when injected into one of the nasal passages during cessation of breathing is called the M. I. O.—the minimum identifiable odor—of the odorous substance.

to this injury. Anterior rhinoscopy in this case showed perforation of the nasal septum, most likely syphilitic.

Sixty persons were studied. Thirty-eight seemed to have a head injury uncomplicated by such factors as contusions about the nose, colds and changes in the nasal mucous membrane. None of those with injury to the frontal region of the skull showed any olfactory involvement. One patient with direct injury to the side of the head (a stab by a screw-driver in the left parietal area) showed olfactory involvement on the side of injury. Two patients with injury to the parietal area showed olfactory involvement on the side of the brain which undoubtedly suffered contrecoup injury. Three patients had almost complete anosmia following occipital injuries.

Dr. Elsberg and his co-workers [4] advised the use of coffee and citral for clinical olfactometry. Coffee is considered by them to stimulate the olfactory nerves alone, without having any effect on the trigeminal nerves. Citral likewise, when used in the small volumes needed for the blast injection test, has no effect on the trigeminal nerves.

Three cases are presented in which anosmia occurred after occipital fractures. There was no evidence of nasal bleeding or contusions about the face.

CASE 1.—J. L., a Negress aged 48, was admitted to the hospital on Aug. 15, 1936. She was struck by an automobile and was unconscious for approximately one hour, recovering consciousness in the hospital. She was sufficiently rational when seen in the emergency ward to complain clearly of headache in the front and back of the head.

There was a laceration of the occiput. There was no orificial bleeding and no localizing neurologic sign, the only finding being a moderate stupor. Roentgen examination of the skull showed diastasis of the right portion of the lambdoid suture, extending as a fracture to the right middle fossa. Spinal tap done at the time of the patient's admission showed a bloody fluid. The Kahn reaction of the blood was negative.

Olfactometry was done two weeks after the patient's admission. She stated that she had always been able to smell perfectly. She did not complain of a cold in the head during the present examination. Anterior rhinoscopy showed the mucous membrane over both inferior turbinates to be hyperplastic.

The patient had almost complete anosmia; coffee and lemon were not perceived by sniffing. When a can of ether (with its label facing her, which she evidently read) was given her to sniff, she identified the substance within as ether. A sniff test with benzene elicited the response of "smells funny." She was not able to perceive alcohol on sniffing.

The fact that she had answered "ether" after sniffing at the can of ether following the reading of the label showed that she was not malingering. She undoubtedly had a contrecoup injury of the frontal or temporosphenoid lobes with involvement of the olfactory pathways.

4. Elsberg, C. A.; Brewer, E. D., and Levy, I.: The Sense of Smell: The Odorous Substances to Be Used for Tests of the Olfactory Sense, Bull. Neurol. Inst. New York **4**:286 (Oct.) 1935.

CASE 2.—W. G., a Negro aged 40, was admitted to the hospital on June 6, 1936, in a markedly comatose state. There was a hematoma over the occipital region of the skull. There was no orificial bleeding. The pupils were equal and reacted to light and in accommodation. There was no rigidity of the neck. The reflexes were generally exaggerated. There was incontinence of urine. No localizing neurologic signs were elicited.

Roentgen examination of the skull showed comminuted horizontal fractures of the left portion of the occipital squama and of the left parietal, temporal and sphenoid squamae.

Spinal tap at the time of the patient's admission yielded a markedly bloody spinal fluid.

On June 9 there was rigidity of the neck. Kernig's sign was present bilaterally. The spinal fluid was bloody.

On June 18 the sensorium was still clouded. The spinal fluid was pink and turbid. The Kahn reaction of the blood was negative.

On June 20 the patient was up and about the ward.

On June 25 he was discharged.

No olfactory tests were done during the patient's stay in the hospital because of the lack of cooperation. He later returned to the follow-up surgical clinic complaining of inability to smell any odor since the injury to his head.

Olfactometry was done on August 1. Anterior rhinoscopy showed that the nasal septum was deviated to the left.

The patient was unable to perceive the odor of coffee or lemon when given in blast injections of 30 cc. monorhinally. He was likewise unable to perceive these odors by sniffing. He was then told that the substances in the two bottles were coffee and lemon. He thought that he identified the odor of coffee when a blast injection of 30 cc. was given into the right nostril (i. e., after being told that he was going to smell coffee). When told that he was going to smell lemon, he thought that he perceived a lemon odor when a blast of 60 cc. of citral was injected into the right nostril. (Sixty cubic centimeters of pressure can be built up in the bottle by filling it with two loads of 30 cc. of air.) He said that he perceived no odor on sniffing at alcohol, ether and benzene.

CASE 3.—E. B., a Negro aged 35, with a history of falling and striking the occiput, was admitted to the hospital on Oct. 22, 1936, the date of injury. He was unconscious on admission. There was no evidence of alcoholism. He reacted to painful stimuli. There was a 2 inch (5 cm.) laceration of the scalp in the right occipital region.

The left pupil was 3 mm. in size and fixed to light, and the right pupil was 2 mm. in size and reacted to light. There were no paralyses and no pathologic reflexes. Spinal puncture yielded a pink fluid. A roentgenogram showed a vertical linear fracture on the right side of the occipital bone.

The following day it was felt that the patient was conscious and rational. The left pupil was still dilated. The patient was discharged on November 2.

He returned on November 16 for olfactometry. The left pupil was still larger than the right, both reacting sluggishly to light. The Kahn test of the blood taken while the patient was in the hospital was 4 plus.

Anterior rhinoscopy showed the nasal mucosa to be congested. The septum was slightly deviated to the left. There was a small amount of mucoid secretion in the rhinal cavities.

The patient complained of tinnitus and difficulty in hearing with the left ear since injury. He also complained of loss of the sense of smell and of a lack of taste to his food.

On one occasion a blast of 30 cc. of coffee was called "stink" when injected into the right nostril. The patient perceived no odors again on further blast injections of coffee or citral into the right or left nostril.

On sniffing at ether, alcohol and benzene with the left nostril he said that he did not smell anything. On sniffing with his right nostril, he said that alcohol smelled like "whisky," benzene smelled "bitter" and ether smelled "strong."

The patient undoubtedly suffered contrecoup injury to the olfactory centers, with possibly greater damage on the left side. The neurologic findings on the left side may substantiate this claim.

MECHANISM OF INJURY

The following mechanism of injury is suggested as the possible etiologic factor in the production of anosmia in the foregoing three cases:

The olfactory nerve arises from a small area of nasal mucous membrane in the upper portion of the nasal septum and the adjacent upper portion of the superior nasal concha. Fine filaments of this nerve perforate the cribriform plate of the ethmoid bone and enter the corresponding olfactory bulb which lies directly on this plate. The central olfactory tract connects the olfactory bulb by means of the lateral and medial olfactory striae with the cortical center for smell, which is located near the tip of the temporosphenoid lobe of the hippocampal gyrus.

Each olfactory bulb is connected with the hippocampal gyrus of its own side by means of the lateral olfactory striae and also with the hippocampal gyrus of the other side by means of the median olfactory striae through the anterior commissure. The lateral olfactory striae are considered to contain a predominately greater number of the secondary fibers and to be more important than the median striae for smell.

When the anterior fossa of the skull is traced backward, it is seen on each side to drop precipitously over the shelving edges of the lesser wings of the sphenoid bone onto the greater wings of this bone. In the recesses between the greater and the lesser wings lie the tips of the temperosphenoid lobes. The lateral olfactory striae and the anterior portion of the hippocampal gyri might conceivably lacerate in a contrecoup injury against these shelving edges of the lesser wings of the sphenoid bone. In a contrecoup injury of the brain the fine olfactory fibers, being exposed on the undersurfaces of the frontal lobes, must come in for a greater degree of injury than if they were buried deeply in the substance of the frontal lobe. Anosmia following occipital injury to the skull might be explained by means of these mechanisms.

Hilton [5] stated in his classic text, "Lectures on Rest and Pain," that:

> When the blow is received at the posterior part of the skull, the whole mass of the brain being driven forwards from the momentum given to it by the blow upon the bones of the skull, the under surface of the anterior part of the brain rubs over the depressed and elevated surfaces which constitute the anatomical features of the internal base of the skull.

Collet [6] explained the occurrence of anosmia after occipital blows in the following manner:

> Traumatic anosmia is found especially following injury due to falls on the back of the neck and occasionally following falls on the face. In the first case there is brought about a tearing or pulling of the olfactory fibers through the process of inertia, or perhaps a small bloody effusion compresses the olfactory fibers following the tearing of the vessels which accompany them.

Two anatomic facts appear to him to dominate the pathologic structure of the olfactory nerve. These are: the fineness of the olfactory filaments transversing the olfactory plate and the presence of olfactory (primary) neurons in the nasal mucous membrane.

Ogle [7] first described cases of anosmia following blows or falls on the posterior portions of the head.

Legg [8] reported the case of a man aged 36, who fell on the right posterior parietal region of the skull. He was unconscious for one-half hour and bled from his left ear. Examination of the sense of smell after one week showed perversion but not complete loss of this sense. The author did not know whether to ascribe the loss to a tearing of the olfactory filaments or to involvement of the temporosphenoid lobes of the brain. He believed that his was the sixth case of anosmia following blows to the posterior portions of the head to be mentioned in the literature.

Helsmoortel, Nyssen and Thienpont [9] referred to an investigator, Fugerio, who in 1887 described a case in which auditory and olfactory hallucinations developed following a fall on the occipital region of the skull. Autopsy showed atrophy of the hippocampal convolutions. He ascribed this to contrecoup action. (I have been unable to find this case in the indexes of the medical literature at my disposal.)

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5. Hilton, John: Lectures on Rest and Pain, ed. 1, London, 1863, p. 25.

6. Collet, F. J.: Étude statistique et étiologique sur l'anosmie, Rev. d'oto-neuro-opht. **11**:1 (Jan.) 1933.

7. Ogle, William: Anosmia: Cases Illustrating the Physiology and Pathology of the Sense of Smell, Med.-Chir. Tr. **53**:263, 1870.

8. Legg, J. W.: A Case of Anosmia Following a Blow, Lancet **2**:659 (Nov. 8) 1873.

9. Helsmoortel, J.; Nyssen, R., and Thienpont, R.: Les troubles olfactifs dans les traumatismes cranio-cérébraux, Rev. d'oto-neuro-opht. **11**:489 (July) 1933.

Bostroem,[10] Laemmele,[11] Helsmoortel, Nyssen and Thienpont [9] and Kindler [12] in recent publications reported anosmia following blows or falls on the occiput.

HIGHER OLFACTORY COEFFICIENTS IN LACERATION OF THE BRAIN

Three cases of injury to the brain are presented, one direct and the other two most likely contrecoup, in which the higher olfactory coefficients were found on the side of injury.

CASE 1.—E. F., a Negro aged 23, was struck on the head by a blunt object and rendered unconscious for about one hour. He walked home after regaining consciousness. He since had had severe frontal headaches. He was admitted to the hospital on Aug. 9, 1936, the day of injury, conscious and rational. Examination showed swelling and tenderness of the scalp in the right parieto-occipital region near the vertex. There was no orificial bleeding and no abnormal neurologic

TABLE 1.—*Results of Blast Injection Tests*

Coffee				Citral			
M. I. O.		Response Elicited		M. I. O.		Response Elicited	
Left	Right	Left	Right	Left	Right	Left	Right
13 cc.	3 cc.	"Not sweet"	"Not sweet"	13 cc.	5 cc.	"Sweet"	"Sweet"

TABLE 2.—*Results of Stream Injection Tests*

Coffee				Citral			
M. I. O.		Duration of Fatigue		M. I. O.		Duration of Fatigue	
Left	Right	Left	Right	Left	Right	Left	Right
10 cc.	5 cc.	2 min.	1.5 min.	18 cc.	5 cc.	1.5 min.	2.5 min.

signs. Spinal tap on August 10 yielded a bloody fluid, and on August 11, a pink fluid. A roentgenogram of the skull showed a fracture of the right frontal, parietal and occipital bones.

Olfactometry was done on August 16, seven days after the patient's admission; anterior rhinoscopy showed hypertrophy of the right inferior turbinate and a septum which was slightly deviated to the right.

Blast injection tests were carried out on August 16 and 18. Coffee and citral were used for both examinations, and the minimum identifiable odor was greater on the left than on the right (table 1).

Stream injection tests [13] were carried out on August 18 (table 2).

10. Bostroem, A.: Ueber traumatische Hirnschädigungen, Wien. klin. Wchnschr. **43**:129 (Jan. 30) 1930.

11. Laemmele, H.: Ueber Geruchsstörungen und ihre klinische Bedeutung, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **130**:22 (Oct. 8) 1931.

12. Kindler, W.: Geruchsstörungen nach Schädelverletzung in medizinischer und sozialer Bedeutung, Med. Welt **10**:150 (Feb. 1) 1936.

13. Elsberg, C. A.: The Sense of Smell: Olfactory Fatigue, Bull. Neurol. Inst. New York **4**:479 (Dec.) 1935.

The patient undoubtedly suffered a contrecoup laceration of the left frontal lobe and possibly of the left temporal lobe, the side which gave the higher minimum identifiable odor.

CASE 2.—J. B., a Negro aged 40, was admitted to the hospital on March 25, 1936. He was found lying on the sidewalk in an unconscious state and suffering from alcoholism.

Physical examination showed an unconscious man with a contusion of the scalp in the left parietal area. The left pupil was larger than the right and did not react to light. There was hemiplegia on the left (including facial paralysis of the upper motor neuron type). The hemiplegia proved later to be hemiparesis and was gone the following day.

There was no orificial bleeding. Roentgen examination of the skull gave negative results. Spinal tap at the time of the patient's admission yielded a bloody fluid; six days later bloody fluid was again obtained.

The patient regained consciousness on the following day. He was confused and irrational for a period of about two weeks.

Olfactometry was done on April 22. The left pupil at this time was still larger than the right and reacted sluggishly to light. The patient complained of dizziness and weakness. Anterior rhinoscopy showed the septum to be deviated to the left, with a spur formation in its lower portion, on the left. Blast injection tests were carried out (table 3).

TABLE 3.—*Results of Blast Injection Tests*

Coffee				Citral			
M. I. O.		Response Elicited		M. I. O.		Response Elicited	
Left	Right	Left	Right	Left	Right	Left	Right
6 cc.	10 cc.	"Coffee"	"Coffee"	4 cc.	20 cc.	"Mint"	"Mint"

The patient was discharged before stream injection tests could be carried out.

The higher minimum indentifiable odor was found on the side on which injury to the cerebrum had produced left hemiparesis (i. e., involvement of the right side of the brain).

CASE 3.—M. G., a Negress aged 22, was admitted to the hospital on July 11, 1936, in a semiconscious and wildly excited state. The history obtained from the family was that the patient had been stabbed in the head with a screw-driver.

Physical examination revealed a small laceration of the scalp in the left parietotemporal area. The right pupil was larger than the left. The patient was unmanageable and had to be controlled by intravenous injection of sodium amytal.

Spinal tap on July 11 and on July 13 yielded a bloody fluid. On July 16 the patient became quieter and began to regain consciousness.

When she became rational it was seen that she had a motor aphasia for speech. She later complained that she could not see things to the right of her. Examination revealed right lateral homonymous hemianopia.

Olfactometry was attempted on July 28; anterior rhinoscopy showed that the nasal septum was slightly to the left. Because of the aphasia, interpretation of responses were confusing. An attempt was made the following day with similar confusion. The patient was discharged on August 3.

She returned on October 16 for examination. Olfactometry by blast injection was done at this time (table 4). There were still slight residuals of the motor aphasia.

An attempt was made to recheck the values by testing with each substance. The patient evidently began to tire of what she called an "unnecessary test." She said she smelled the substances when only from 2 to 4 cc. would be injected into each nostril. Such secondary attempts were stopped, and the patient was requested to return the following day. She did not return.

The marked difference in the minimum identifiable odor on the two sides must furnish, however, some validity to the initial tests. It would have been interesting to carry out stream injection tests to determine the duration of olfactory fatigue because of the likewise high values for the minimum identifiable odor on the right side.

It is likely in this case that there was injury to the left temporal lobe of the brain with involvement of Broca's area, the uncus and the left optic tract lying mesial to it.

TABLE 4.—*Results of Blast Injection Tests*

Coffee				Citral			
M. I. O.		Response Elicited		M. I. O.		Response Elicited	
Left	Right	Left	Right	Left	Right	Left	Right
30 cc.*	15 cc.	"Coffee"	"Coffee"	30 cc.*	15 cc.	"Sweet"	"Sweet"

* The patient did not perceive any odor when 30 cc. had been injected except on one occasion.

Ogle [7] reported a case of aphasia and agraphia following a fit. The aphasia was not so complete as to prevent the patient from making himself understood; there was no paralysis present. This patient was able to smell much better with his right nostril than with his left.

This investigator also described the case of a boy aged 12 years who suddenly lost power in his right side and fell without losing consciousness. He had a fit a few hours later which left him with partial aphasia and incomplete hemiplegia on the right side. He completely lost the sense of smell in the left nostril.

This writer expressed the belief that the lesions producing the aphasia in the two cases implicated also the fibers of the "external root of the olfactory bulb."

Such lateralization (ipsilateral predominance) of the sense of smell has been clearly indicated in the work of Elsberg [14] in the localization of suprasellar tumors and tumors of the frontal lobe of the brain.

14. Elsberg, C. A.: The Sense of Smell: The Value of Quantitative Olfactory Tests for the Localization of Supratentorial Tumors of the Brain; a Preliminary Report, Bull. Neurol. Inst. New York **4**:511 (Dec.) 1935; The Sense of Smell: The Localization of Tumors of the Frontal Lobe of the Brain by Quantitative Olfactory Tests, ibid. **4**:535 (April) 1936.

In the limited number of cases of injury to the side of the head which were presented in this article, a lateralization (ipsilateral predominance) of the sense of smell was indicated.

SUMMARY

Olfactometry was done on sixty patients with acute trauma to the head.

In thirty-eight patients the injury was uncomplicated by such factors as contusions about the nose, colds and changes in the nasal mucous membrane.

Three of the thirty-eight showed almost complete anosmia following injury to the occipital region of the skull.

Injuries about the anterior portions of the head seem to play a secondary rôle in producing disturbances of the sense of smell (i. e., without local injury to the nose or fractures through the cribriform plate).

This loss of the sense of smell following injuries to the back of the head or neck is usually ascribed to contrecoup action on the olfactory fibers lying on the undersurfaces of the frontal lobes.

A new mechanism of injury is suggested in which the lateral olfactory striae and the tips of the temporosphenoid lobes are injured against the lesser wings of the sphenoid bone.

Three cases are presented in which there were injuries to the side of the head. The patient who suffered from direct injury to the parietal and temporal lobes of the brain had higher olfactory coefficients on the side of injury. The two who had contrecoup involvement of the brain showed the higher olfactory coefficients on the side of the injury.

CONCLUSION

1. Falls or blows on the back of the neck and occiput seem to be predominant in producing disturbances or loss of the sense of smell. The occurrence of anosmia after such injuries is not infrequent.

2. Injuries to the front of the head (i. e., without local injury to the nose or fractures of the anterior cranial fossa or cribiform plate) play a secondary rôle in producing disturbances of the sense of smell.

3. Injuries to the side of the head may produce disturbances of the sense of smell. In the limited number of cases presented the higher olfactory coefficients were obtained on the side of the injury.

SIXTY-FOURTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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CONGENITAL DEFORMITIES

Heredity in Congenital Dislocation of the Hip.—By the reproduction of a set of 10 family trees, Faber [1] shows not only that true congenital dislocation of the hip (25 cases) occurs in these families but that dysplasia of the hip joint (73 cases), oblique acetabulum and subluxation are found three times as often as dislocation. This indicates that the taint is four times as strong as would be suspected if only dislocations were sought. Furthermore, parents with simple dysplasia may have children with true dislocation. While true dislocation in this series was much more frequent in the female (5 to 1) than in the male, if one includes the cases of dysplasia the ratio is 1.55 to 1. The father as well as the mother in an affected family may transmit dysplasia or true dislocation. Furthermore, it is probable that unaffected persons in such a family may act as "carriers."

[ED. NOTE.—A study of the distribution of monarticular osteoarthritis of the hip (which is probably often the clinical end-result of such dysplasia) may reveal a long suspected correlation.]

This report of progress is based on a review of 126 pages selected from 181 titles related to orthopedic surgery, which appeared in the medical literature approximately between March 1, 1937 and July 2, 1937.

1. Faber, A.: Ztschr. f. Orthop. **66**:140, 1937.

Arthrography in Congenital Dislocation of the Hip.—Leveuf and Bertrand [2] have frequently found a lengthened articular capsule with a closed portion in the middle in cases of congenital dislocation of the hip. This defect in the capsule is not readily determined clinically, although roentgenograms will show a wide separation of the head of the femur and the acetabulum. By the use of colloidal thorium dioxide, neo-iopax and other radiopaque substances, the authors were able to demonstrate the narrowing or closure of the articular capsule in roentgenograms. Ten cubic centimeters of a 30 per cent solution of the opaque substance was injected into the hip joint, the neede being introduced anteriorly to the head of the femur.

DEVELOPMENTAL DISTURBANCES

Osteitis Fibrosa Disseminata, Areas of Pigmentation and Precocious Puberty in Females.—Five cases of this syndrome are reported by Albright and his co-workers,[3] and illustrations of the pigmented areas and diagrams of the areas of osseous involvement are presented. In addition, reports of 9 strikingly similar cases and 5 suggestively similar ones were found in a search of the literature; the diagnoses in these cases included neurofibromatosis, juvenile Paget's disease, xanthoma, osteodystrophia fibrosa and osteitis fibrosa generalisata. The characteristics of the syndrome are: (1) changes in the bone, (2) brown pigmented areas and (3) endocrine dysfunction. The changes in the bone are spotty in distribution and consist of multiple localized cystlike areas often associated with circumscribed areas of increased density. It is remarkable that the changes show a tendency to be unilateral, or at least regional, i. e., in one entire extremity. The epiphyses often escape involvement when the entire remainder of the shaft is involved. Early fusion of the epiphyses is the rule, associated with precocious bone age, i. e., premature appearance of ossification centers. Microscopic examination of the areas involved usually reveals a notable absence of osteoclasts. Since the surrounding areas of bone are not affected, the condition should be classified as osteitis fibrosa localisata as opposed to osteitis fibrosa generalisata; however, because the lesions are multiple, the designation osteitis fibrosa disseminata has been used. Further differentiation from hyperparathyroidism is based on the facts that the values for serum calcium and inorganic phosphorus are within normal limits and the urinary excretion is not increased. Increased values for serum phosphatase may be found in cases in which there are advanced changes in the bone. Pigmentation is patchy and occurs most frequently over the

2. Leveuf, J., and Bertrand, P.: Presse méd. **45**:437, 1937.

3. Albright, F.; Butler, A. M.; Hampton, A. O., and Smith, P.: New England J. Med. **216**:727, 1937.

sacrum, buttocks and upper part of the spine. The patches do not appear to have the same distribution as the cutaneous nerves. The distribution of the osseous and cutaneous lesions suggests an embryologic or a neurologic disturbance. The former would be more likely if the pigmentation were due solely to melanoblasts of mesodermal origin. Though the distribution of the pigmented areas is such as to suggest a mesodermal origin, the histologic evidence indicates that most of the melanoblasts are of ectodermal origin. This would seem to require an embryologic disturbance affecting both the ectoderm and the mesoderm. The unilateral character of the syndrome is similar to that observed in Ollier's dyschondroplasia, in which there are multiple unilateral enchondromas. Precocious puberty occurs only in the female, suggesting the hypothesis that this part of the syndrome is due to a disturbance in the follicle-stimulating hormone of the pituitary gland. The disease in its complete form must be rare. It is suggested, however, that it may occur in incomplete forms, and in cases in which hyperparathyroidism is suspected to be present this must always be considered. A prognosis of serious disability from fractures seems justified. Roentgen irradiation of the local lesions or of the pituitary gland or of the region of the parathyroid glands has been attempted, but with inconclusive results.

Pathogenesis of Certain Growth Disturbances.—Schneider [4] believes that the aseptic osteocartilaginous necrosis observed in children, e. g., Legg-Perthes' disease, is explained by a disturbance in nutrition. He reviews the various theories proposed in the literature and concludes that three possibilities are present: (1) a vitamin deficiency, (2) an endocrine disturbance with interference with the storage and saturation of vitamins and (3) loss of vitamins following infection. He reviews a large number of personally observed cases in which the blood serum was deficient in vitamin A. He shows the relationship of hypothyroidism and hyperthyroidism to the storage of vitamin A and the gradual injury that may occur to the cartilage and bone following loss of this vitamin.

A possible therapeutic approach through the investigation of vitamin A deficiency is suggested in addition to the commonly employed symptomatic mechanical therapy.

Köhler's Disease of the Tarsal Scaphoid. —Smets,[5] of Brussels, concludes from a clinical study and from a review of the cases reported in the medical literature that so-called Köhler's disease is a normal variation in ossification. His reasons for this are: 1. The lesion is usually found on both sides. 2. In most cases there are no symptoms, and the condition is an incidental roentgenographic finding. 3. The

4. Schneider, E.: Arch. f. klin. Chir. **188**:91, 1937.

5. Smets, W.: Bull. Soc. belge d'orthop. **7**:65, 1936.

lesion heals spontaneously. 4. Usually alterations in ossification can be found in other parts of the body. 5. There is a familial tendency to this condition which is occasionally shown in twins. At times, as the author demonstrates, this variation in ossification is a generalized phenomenon.

OSSEOUS CHANGES IN CERTAIN DISEASES

Osseous Changes in Sickle Cell Anemia.—Diggs and his co-workers [6] conclude from the study of 30 cases of sickle cell anemia, some of which were studied microscopically, that the gross, microscopic and roentgenographic appearances of the bones indicate that the bone marrow is primarily involved. Two factors appear to be working in opposite directions. One factor is hyperplasia, which tends to increase the volume of the marrow at the expense of bone, and the other is sclerosis, which tends to replace the marrow and to substitute osteoid tissue or new bone. The excessive and abnormal growth activity of the marrow has, as a rule, no significant effect on the bony cage within which it is confined, and such effects as it does have are maximal in the bones which are normally engaged in the formation of blood cells, such as the skull and the cancellous bones of the trunk. In these bones osteoporosis is dominant. In the long bones in which normal hematopoiesis does not occur sclerosis is dominant. The combination of marrow-expanding and marrow-replacing processes leads, if the patient lives long enough, to gross anatomic derangements in the structure of the bone.

Osseous Changes in Leukemia.—Connor [7] states that the roentgenographic appearance of bones of patients suffering from leukemia may be similar to that of bones of persons with osteomyelitis. The differential diagnosis is dependent on a study of the blood.

Changes in the Growing Skeleton After the Administration of Bismuth.—The roentgenographic changes produced in the skeleton of infants and children by bismuth are described by Caffey,[8] and the similarity of these changes to those produced by lead is pointed out. The most conspicuous microscopic changes are: (1) an increase in the calcified cartilaginous matrix in the zone of primary calcification, accompanied by a decrease in the endosteal bone usually present in this region, and (2) later active deposition of bone in the deeper parts of the lesion, which, owing to the increased cartilaginous framework, results in a zone containing a larger amount of bone than is normal. Minor differences in the microscopic changes produced by lead and bismuth are described.

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6. Diggs, L. W.; Pullian, H. N., and King, J. C.: South. M. J. **30**:249, 1937.

7. Connor, C. L.: Am. J. Cancer **29**:20, 1937.

8. Caffey, J.: Changes in Growing Skeleton After Administration of Bismuth, Am. J. Dis. Child. **53**:56 (Jan.) 1937.

Osseous Changes in Recklinghausen's Neurofibromatosis.—Norgaard,[9] of Copenhagen, reviews the osseous changes observed both in personally observed cases of Recklinghausen's neurofibromatosis and in those cases reported in the literature. These changes may be of importance in the differential diagnosis when the usual symptoms of the disease are not very evident. Kyphoscoliosis is present in most of the cases due to osseous changes, which resemble those seen in osteomalacia. Periosteal cysts are frequently seen. There may be increased or diminished growth of parts of the skeleton. Roentgenograms illustrating these osseous changes accompany the article.

OSTEOMYELITIS

Acute Osteomyelitis.—Sorrel,[10] in a discussion of the treatment of acute osteomyelitis, states that the immunologic forms of therapy offer little at present. Osteomyelitis, with its staphylococcic septicemia and localization in bone, is different from many other infections. Antibodies are produced only slowly or not at all. None of the methods so far used —vaccine therapy, transfusions of blood from immune subjects, bacteriophage or staphylococcus antitoxin—have decreased the use of surgical treatment for osteomyelitis. Except in cases of staphylococcic septicemia with few symptoms referable to the bone, immediate surgical intervention is indicated. The type of operation will depend on the nature of the osteomyelitis.

[ED. NOTE.—While little benefit has been observed from the immunologic forms of treatment, there is a tendency toward greater conservatism in treatment.]

Diaphysial Resection in Osteomyelitis.—Sorrel [11] reports the results of resection of the diaphysis in 32 cases of acute osteomyelitis. He feels that the operation has a definite place in cases of acute widespread osteomyelitis in a single bone in which the patient is gravely ill and in which in all probability the bone has become necrotic over a large area. He reserves simple incision for subperiosteal abscess and simple opening of the bone for a localized central abscess. Of 32 patients subjected to diaphysectomy, chiefly of the tibia and the femur, 4 died, 6 could not be traced and 1 underwent operation too recently for comment. The remaining 21 patients were completely cured, with regeneration of the bone; growth proceeded normally, and normal function was restored. In 4, pseudoarthrosis resulted, necessitating later grafting of the area.

[ED. NOTE.—Diaphysectomy is rarely advisable except in bones that are not necessary for function. The danger of nonregeneration is too great.]

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9. Norgaard, F.: Acta radiol. **18**:460, 1937.
10. Sorrel, E.: Cir. ortop. y traumatol., Habana **5**:3, 1937.
11. Sorrel, E.: Bull. Soc. belge d'orthop. **9**:319, 1937.

Syphilitic Osteomyelitis.—Two cases of syphilitic osteomyelitis are reported by Westermark and Hellerström [12] in which a preliminary diagnosis of osteogenic sarcoma had been made. The first patient, aged 25, had a warm pulsating tumor of the soft part over the anterior aspect of the left tibia of six months' duration. Roentgenograms showed a destructive lesion, not sharply outlined, with spicule formation in the upper part of the tibia The Wassermann reaction was positive, and healing occurred under antisyphilitic therapy. The second patient, aged 33, had a gradually increasing swelling on the left tibia, with pulsation and local heat. Roentgenograms showed a destructive process with spicule formation. In this case, also, the Wassermann reaction was positive, and healing took place under antisyphilitic treatment. The ability of syphilis to simulate an osseous neoplasm makes a careful study imperative.

TUBERCULOSIS

Pott's Disease in Adults.—McKee [13] compares the end-results in cases of tuberculosis of the spinal column in which conservative methods of therapy were employed with those in which operative fixation was done. Good clinical results were obtained in 70 per cent of the former, with late abscess formation in only 4 per cent, while such results were obtained in only 32 per cent of the latter, with late abscess formation in 40 per cent. McKee concludes that a graft should serve as a local internal splint and should be employed only after consolidation has taken place.

[ED. NOTE.—The efficacy of spinal fusion is dependent largely on the treatment of the patient for the systemic disease.]

Tuberculosis of the Knee.—Hellner [14] analyzes 87 cases of tuberculosis of the knee seen at the surgical clinic of Munster between 1925 and 1936. In 20 cases tuberculosis was thought to be present, but the condition was later proved to be nontuberculous. Diagnosis was established by the clinical course, inoculation of guinea-pigs or excision of tissue. No method of diagnosis was found applicable to all cases. Exploratory excision of tissue did not have an unfavorable influence in any case. Conservative treatment, in the author's opinion, is not justified except in cases of early tuberculous hydrops in which motion is still present and does not lead to cure. Resection of the joint in cases of fungoid tuberculosis and amputation in those cases in which extensive secondary infection is present are the treatments of choice. No figures are given for the end-results.

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12. Westermark, N., and Hellerström, S.: Acta radiol. **18**:422, 1937.
13. McKee, G. K.: Brit. J. Surg. **24**:456, 1937.
14. Hellner, H.: Arch. f. klin. Chir. **188**:215, 1937.

Operative Treatment of Tuberculosis of the Knee Joint.—Tregubov's [15] conclusions concerning the treatment of tuberculosis of the knee joint are based on the results obtained in 609 cases during the period between 1921 and 1936, in 147 of which surgical measures were employed. He feels that the best results are obtained by operative treatment. Although adolescents and adults are the most suitable subjects for operation, excellent results have also been obtained in elderly persons. The period of abatement of the tuberculous process is the best time to perform the operation, which should be a simple one, aiming chiefly at the formation of ankylosis, although the foci in the bone should be thoroughly removed by curettement and the cavity filled with bone chips. It is important to fix the knee in a position of slight flexion. A plaster cast is applied from the pelvis to the toes. At the end of approximately six weeks the patient is permitted to walk on crutches and to bear weight on the affected leg. Three months after the operation the plaster bandage is shortened. During the following three months the patient bears weight freely on the leg. At the end of this time a removable cast is applied. Of 147 patients operated on, 2 died, 1 from accidental infection and the other from tuberculous meningitis. In both cases, however, the process in the knee joints healed. Of the remaining 145 patients, only 55 appeared for examination. Forty-six of these obtained good results and have returned to a normal life. In 2, shortening amounted to 7 cm., but in the others it averaged between 3 and 4.5 cm. The author strongly condemns the so-called nailing operations.

On the basis of a follow-up study of patients treated in a tuberculosis sanatorium, 75 by conservative measures and 30 by fusion, Lampadius [16] advocates conservative therapy in preference to operation. His conservative treatment consists of rest, diet and the use of a plaster bed. Fresh air rather than direct sunlight is stressed. All but 2 of the patients treated in this manner improved. Healing occurred in 28 with a gibbus and in 37 without a gibbus. Diagnosis was confirmed by roentgenographic examination for the most part, and the course was followed by determinations of the sedimentation rate. At the time of reexamination there were 30 patients on whom operative treatment had been used (Albee's technic). In addition to this group, 4 had died of the operation and 6 had died since discharge from the hospital (3 of unknown causes). The author states that in the 30 patients the "good and bad results balanced."

[ED. NOTE.—The statistical material does not lend itself to satisfactory comparison as presented in the paper. No systematic tabulation indicative of the age, duration, presence of tuberculosis elsewhere or the clinical severity of the lesion in the different groups is available.]

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15. Tregubov, S.: J. Bone & Joint Surg. **19**:734, 1937.

16. Lampadius, H.: Ztschr. f. Orthop. **66**:89, 1937.

THE BACK

Spinal Deformity Following Tetanus.—Roberg [17] presents the results of a study of all of the factors which may lead to spinal deformity following tetanus. Sixty-three cases, comprising all of those reported in the literature up to the present, were reviewed. Photographs, roentgenograms and charts have been included. Kyphosis of the vertebral column may follow tetanus with or without demonstrable fracture of the vertebral body. Therefore, initiating this deformity is the contraction of certain muscle groups during tetanic convulsion. Although there is a greater tendency for vertebral fracture to occur in adults, the majority of cases of posttetanic kyphosis occur in adolescents of an age corresponding to those affected with juvenile kyphosis. Posttetanic spinal deformity in adults is the result of a peculiarly severe and prolonged attack of tetanus.

Lesions of the Intervertebral Disk.—Barr [18] reports 40 cases in which lesions of the intervertebral disk were verified at operation. The symptoms and signs of rupture of the intervertebral disk depend on the location of the lesion. Lesions in the lumbar region produce a characteristic clinical syndrome. In 26 of the cases in the reported series the involved disk was between the fourth and the fifth lumbar vertebra. The youngest patient was 20 years of age and the oldest 58. Thirty-five of the patients were males. Thirty patients gave a history of trauma. The chief symptom was pain along the sciatic nerve and its branches, and in 34 cases the pain was unilateral. There was a list of the lumbar portion of the spine in 26 cases. Reflexes were normal. Sensory disturbances were present in 17 cases. Roentgenographic study showed no narrowing of the intervertebral disk in 25. Roentgenographic examination following the injection of iodized poppy-seed oil 40 per cent was carried out in 39 cases and showed total block in 5, partial in 30 and a questionable filling defect in 1. Lumbar puncture showed an elevated total protein content in the spinal fluid in 35 cases. The dynamics of the spinal fluid were normal in 36. The findings at laminectomy varied greatly. The extruded nucleus pulposus was usually removed without undue difficulty. Spinal fusion was performed on 12 patients at the time of laminectomy to insure greater stability where articular facets had been removed. Twenty-nine patients were completely relieved of pain; 2 had a disabling motor weakness or paralysis, and 2 had died, 1 from uremia and 1 from pneumonia. The remaining patients were not followed sufficiently long for comment.

Chronic Traumatic (Postural) Destruction of the Lumbosacral Intervertebral Disks.—Williams [19] believes that mechanical alterations of the

17. Roberg, O. T., Jr.: J. Bone & Joint Surg. **19**:603, 1937.
18. Barr, J. S.: J. Bone & Joint Surg. **19**:323, 1937.
19. Williams, P. C.: J. Bone & Joint Surg. **19**:690, 1937.

lower part of the spine which cause an uneven distribution of weight on the intervertebral disks may produce early pathologic degeneration of that portion of each disk which is under abnormal pressure. When the patient is in the erect position this pressure is exerted only on the posterior and lateral margins of disks. The symptoms usually occur between the ages of 30 and 40 and consist of a relaxed attitude and poor muscular tonus and a history of fatigue and pain, the latter being aching in character. The pathologic process is manifest by degenerative changes involving the annulus fibrosus and the nucleus pulposus and by subluxation of the facets, with resulting degenerative arthritic changes. Roentgenographic studies reveal pelvic obliquity, narrowing of the lumbosacral joint space, subluxation of the lumbosacral facets and frequently hypertrophic lipping and sclerosis involving the articulations and occasionally the vertebral bodies. Treatment varies according to the age of the patient and the severity of the symptoms. Pelvic obliquity should be compensated by adding a lift to the heel of the shoe. Exaggerated lordosis of the lumbosacral portion of the spine in a man under the age of 50 and in a woman under the age of 40, whose roentgenograms reveal narrowing of the posterior margins of the disks and whose symptoms are chronic, is treated by postural exercises. All foci of infection should be removed and high heels replaced by medium or low heels. When the symptoms are acute, a plaster jacket is applied with the patient in a standing position and with the spine flexed so that the lordosis is eradicated. This jacket is later replaced by an orthopedic corset. When all symptoms have disappeared, postural exercises are instituted. In an older patient, postural exercises and a brace to support the lower part of the spine and to eradicate the lordosis are indicated. When the deformity fails to respond to such conservative treatment, surgical measures should be employed.

Operative Treatment for Pain Low in the Back.—After reviewing the various types of operations which have been described for relief of pain low in the back, Compere [20] states that the majority of patients with this type of pain can be relieved without operative intervention. Operation should be performed only after the diagnosis has been accurately established and the presence of an osseous neoplasm or a neurologic lesion has been excluded. Definite indications for operative treatment include tuberculosis or chronic sclerosing osteomyelitis of the lumbosacral or sacro-iliac joints, primary malignant neoplasms, lesions of the spinal cord, spondylolysis or spondylolisthesis. The operation is contraindicated in patients with chronic infectious arthritis, in patients with a psychiatric background and in those seeking financial compensation for injuries. Compere believes that operation is justified for chronic

20. Compere, E. L.: J. Bone & Joint Surg. **19**:749, 1937.

strain low in the back in the absence of definite roentgenographic evidence of a local pathologic process if conservative therapy has failed to bring relief and the patient has to do manual labor to earn a living. The author considers arthrodesis the operation of choice. If sciatic neuritis is present, excision of the articular facets on each side between the fourth and the fifth lumbar vertebrae and the fifth lumbar vertebra and the sacrum is advised.

CHRONIC ARTHRITIS

Evaluation of Diagnostic Tests in Rheumatoid Arthritis.—Short and his co-workers [21] review the various laboratory procedures employed in the diagnosis and evaluation of chronic arthritis. The blood sedimentation test was found to be positive in 92 per cent of 49 patients with active rehumatoid arthritis. The Schilling count was helpful in 87 per cent. Positive readings were obtained with the Vernes test in 58 per cent, and the streptococcus agglutination test was positive in 53 per cent. The authors conclude that for ease of performance and accuracy the blood sedimentation test is the most satisfactory test for the recognition and evaluation of rheumatoid arthritis.

VASCULAR DISTURBANCES OF THE EXTREMITIES

Value of Sympathectomy in the Treatment of Vascular Disease.—The results of sympathectomy in Raynaud's disease and thrombo-angiitis obliterans are discussed by Smithwick.[22] The various operative approaches recommended and the stages of the diseases at which optimum results may be obtained from operation are described in detail. In summary, the author states that preganglionic section in cases in which there are marked vascular spasms of the extremities, e. g., in Raynaud's disease, has given satisfactory results which could not be obtained by ganglionectomy. In certain cases of thrombo-angiitis obliterans peripheral nerve block is satisfactory, and in a smaller number preganglionic section gives the desired results.

Treatment of Diabetic Gangrene.—Samuels [23] advocates complete rest with the affected extremity in a horizontal position for the treatment of impending diabetic gangrene. Superficial infections should be treated by gentle irrigation through sterile dressings. The natural heat of the limb should be preserved, but excessive heat applied externally does harm. A 2 or 3 per cent hypertonic saline solution should be given intravenously. The author observed no improvement from the use of

21. Short, C. L.; Dienes, L., and Bauer, W.: Rheumatoid Arthritis: Comparative Evaluation of Commonly Employed Diagnostic Tests, J. A. M. A. **108**: 2087 (June 19) 1937.

22. Smithwick, R. H.: New England J. Med. **216**:141, 1937.

23. Samuels, S. S.: Surgery **2**:225, 1937.

negative pressure or from ganglionectomy or sympathectomy. Ringworm infections should be treated thoroughly, since they produce lesions from which other infections start. The indications for amputation are spreading gangrene or spreading infection. The author prefers for amputation a simple circular incision in the lower third of the femur with immediate closure of the stump.

THE SHOULDER

Painful Shoulder.—Ferguson [24] reviews the treatment of soft tissue lesions involving the subacromial or subdeltoid bursa and the supraspinatous tendon in 200 patients. The following lesions are discussed: (1) acute traumatic bursitis, (2) acute bursitis with calcifications, (3) subacute bursitis with calcification, (4) chronic bursitis and (5) tendinitis or obliterative bursitis. For the treatment of acute traumatic bursitis, the author uses immobilization of the shoulder by means of strapping with adhesive tape, an illustration of which is given in the text. After two or three days he uses moist or dry heat. Immobilization should be continued for a week or ten days, followed by exercises which gradually increase the range of motion until normal function is reached after a period of three or four weeks. The author believes that the prognosis is good provided immobilization is maintained long enough. Treatment for acute subdeltoid bursitis with calcification consists mainly of relieving the tension in the bursa by incision, procaine hydrochloride being used to obtain anesthesia. With the relief of the tension, the patient experiences immediate comfort. The incision is enlarged, and as much of the calcified material as possible is removed with a curet. A simple pressure dressing is applied, and a sling is adjusted. Immediate relief is followed by recovery without disability in one or two weeks. Subacute bursitis with calcification presents a different roentgenographic picture, for the areas of calcification are not usually so large or so dense as those in acute bursitis and are located on top of the greater tuberosity rather than along its lateral edge. The pathologic process consists of an area of calcification in the floor of the bursa. Treatment should be conservative. Operation is contraindicated. Baking and diathermy are effective in relieving the pain in about half the cases, but in those cases in which relief is not obtained by such measures injections of from 20 to 30 cc. of 1 per cent solution of procaine hydrochloride in the region of the bursa are often effective. After the acute symptoms have subsided, active exercises within pain limits are of most value. The prognosis for eventual recovery is good. The roentgenographic picture of chronic bursitis consists of changes in the greater tuberosity, with excrescences and small defects at the insertion of the supraspinatus

24. Ferguson, L. K.: Ann. Surg. **105**:243, 1937.

tendon on the greater tuberosity. Trauma may also cause the development of villi. The treatment is divided into conservative and operative. Conservative treatment consists of rest and the application of heat. However, in a few patients in whom the symptoms persist, incision of the bursa and excision of the offending villi or excrescences are advised. In Ferguson's hands this method of treatment was successful in 4 cases. The prognosis is usually good. As a rule, under conservative therapy relief from symptoms may be obtained in from three to four weeks. When symptoms persist beyond this time, operation is indicated, with the prospect of relief from symptoms in another three or four weeks. In cases of tendinitis or obliterative bursitis treatment with heat and rest is slow and often discouraging. A second method has proved more successful, namely, the injection of from 20 to 30 cc. of 1 per cent solution of procaine hydrochloride into the region of the subdeltoid bursa. After the injection, manipulations are carried out carefully. First internal and external rotation are done, followed by circumduction at the shoulder, with a gradually increasing range of motion. During the manipulation there may often be a palpable and even an audible snap. If the manipulation is too painful, sometimes a second injection of procaine hydrochloride is necessary. In some cases the normal range of motion may not be recovered for from six to twelve months.

Alar Scapula.—Berkheiser and Shapiro[25] report 4 cases of alar scapula resulting from traumatic paralysis of the serratus anterior muscle. Injury to the long respiratory nerve of Bell was caused by violent pulling movements (lifting window, scrubbing, etc.) of the upper part of the arm in each instance. For treatment, the arm and thorax were incased in plaster with the elbow flexed 90 degrees and the arm externally rotated 180 degrees and abducted 90 degrees for three months. In this position the scapula was pressed against the wall of the chest, and the serratus anterior muscle was relaxed. Complete recovery was observed in these cases.

THE NECK

Cervical Rib and Scalenus Anticus Syndrome.—The term "scalenus anticus syndrome" has been suggested for a condition characterized by pain, circulatory disturbances and trophic changes in the upper extremities resulting from movements of the head, neck and shoulder girdle, in the absence of roentgenographic evidence of a cervical rib.[26] The clinical picture presented by cervical ribs is very similar. The size of a cervical rib is no index to the severity of the symptoms it produces since the determining factor is its relation to adjacent structures, the

25. Berkheiser, E. J., and Shapiro, F.: Alar Scapula: Traumatic Palsy of Serratus Magnus, J. A. M. A. **108**:1790 (May 22) 1937.

26. Craig, W. M., and Knepper, E. A.: Ann. Surg. **105**:556, 1937.

most important of which is the scalenus anticus muscle. It is this muscle that compresses the subclavian artery and the brachial plexus against the cervical rib. The symptoms of compression of the brachial plexus and subclavian artery are usually pain, atrophy, numbness or circulatory changes, consisting of cyanosis, ulcers and rarely gangrene. Although the pain may be more or less continuous, it is invariably exaggerated by rotation of the head or by a forcible downward pull of the shoulder. Circulatory symptoms may manifest themselves by a dusky hue of the arm and hand as compared with the opposite side. Diminution in volume of the radial pulse is common. The pulse can be decreased or obliterated by having the patient elevate the chin or rotate the head to the affected side on inspiration. Treatment for the relief of symptoms of cervical rib and of the scalenus anticus syndrome are the same. The operation which has proved of the greatest value for both conditions is division of the scalenus anticus muscle through an anterior approach. In cases of cervical rib, after the muscle is divided the cervical rib is examined, and if it is causing no pressure from behind further operative treatment is unnecessary. However, if the cervical rib or tendinous attachment to the first rib seems to be compressing the brachial plexus from behind, a portion of the rib and tendon can be removed. Six cases of the scalenus anticus syndrome are reported.

POSTURE

Postural Deformities of the Anteroposterior Curves of the Spine.—Wiles,[27] in the current Hunterian lecture, reviews the neuromuscular physiology of erect posture. He points out that ligaments limit the extremes of motion only and play no part in the normal regulation of posture. In most instances of faulty posture the error lies in postural reflexes and rarely in muscular weakness. He lists the chief etiologic factors producing postural deformities as undernutrition, rapid growth and psychologic maladjustment. A series of measurements were taken of the pelvic inclination by a simple inclinometer set on the anterior superior and posterior superior iliac spines in a large series of normal persons. Wiles concludes that the inclination of the pelvis is controlled almost entirely by the muscles surrounding the hip joints. Variations in posture are limited, since the center of gravity must fall within the area occupied by the feet. Two components of faulty posture are commonly seen: (1) alteration in pelvic inclination and (2) changes in dorsolumbar kyphosis. Wiles considers a flat back a postural deformity; instead, moderate lordosis of the upper part of the lumbar region should be sought. Treatment is divided into three stages: (1) restoration of mobility, (2) acquisition of voluntary control of the correction and (3) establishment of new reflexes which will maintain the correct posture.

27. Wiles, P.: Lancet **1**:911, 1937.

[Ed. Note.—No universally satisfactory definition of good posture can be formulated. What is meant in simple terms is efficient mechanical use of the body habitually. Most students of this problem will question the accuracy of the author's measurements, believing that pelvic inclination at present is a variable factor, changing with activity and not susceptible to exact measurement by such simple means as he describes. The paper is a distinct contribution to the knowledge of posture and merits careful reading.]

Neoplasm.—Dujovich and Shraer [28] report 2 cases of periosteal lipoma in patients 50 and 60 years old, respectively. Both the tumors, one on the rib and one on the humerus, were extirpated without difficulty, and convalescence was uneventful. This type of tumor is adherent to the periosteum by a pedicule, either primarily or secondarily. As a rule, it is symptomless, as were the tumors observed by the authors. Because of the location, such a growth is at times mistaken for a malignant osseous tumor. It grows slowly, and extirpation is the only method of treatment. The most frequent site is on the skull, next on the femur and then on the vertebral column. A full review of the literature is given.

Roentgen Evidence of Malignant Processes in Bone.—A roentgenographic study of vertebrae affected with metastatic cancer did not show the majority of the osseous lesions. Sections of vertebral bodies were removed by Snure and Maner [29] and replaced with muscle or paraffin; the defects could not be seen in roentgenograms. The majority of the bone markings seen in roentgenograms are due to cortex. The spongiosa may be the site of metastases without being evident roentgenographically. These same destructive changes in the marrow space due to infection may likewise not be visible roentgenographically.

Synovioma.—A detailed report is given by Coley and Pierson [30] of 15 cases of synovioma, with a review of 20 cases from the literature. The tumor described is malignant and occurs in or about the joints. It tends to recur after excision and often to metastasize to the lungs. It may occur at any age. The microscopic appearance is that of an endothelioma or mesothelioma showing typically a villous glandlike appearance. Clinically, the tumor is usually firm, well circumscribed, homogeneous and not particularly tender and occurs frequently near the knee joint. Diagnosis, however, has seldom been made until pathologic examination of the tumor after operation. In the 35 cases reviewed, 30 per cent of the patients survived only five years and 40 per cent only three years. No patient survived more than ten years. The

28. Dujovich, A., and Shraer, M.: Semana méd. **1**:183, 1937.
29. Snure, H., and Maner, G. D.: Radiology **28**:172, 1937.
30. Coley, B. L., and Pierson, J. C.: Surgery **1**:113, 1937.

treatment advised is wide excision if the condition is suspected at the first operation, with amputation on recurrence after local removal. Treatment by irradiation is disappointing as this type of tumor is not radiosensitive. Thus far, early treatment appears to have been too conservative, rendering later radical measures ineffectual.

Fehr [31] adds reports of 4 more cases of synovioma to the 19 reported in the literature (mostly American). He recalls the malignant characteristics of this sarcoma which arises from the synovial tissue of the joint capsule. Only early amputation seems of any permanent value. The tumor grows slowly and metastasizes to the lung.

Epithelial Bone Cysts.—Bissell and Brunschwig [32] add reports of 2 cases of squamous epithelial bone cyst to the 4 reported in the medical literature. Both of his patients gave a history of preceding trauma to the distal portion of the finger in which the cyst subsequently developed. Curettement of the cystic cavity resulted in cure in both patients. The authors believe that these cysts develop from traumatic transplantation of squamous epithelium in or on the bone. An embryonic rest of the epithelium is a possible but less likely cause.

MISCELLANEOUS

Posttraumatic Painful Osteoporosis.—Discussing posttraumatic osteoporosis, Middleton [33] states that the results of sympathectomy are transitory and that ganglionectomy probably offers more hope for beneficial results. He believes that the administration by ionization of certain parasympathetic stimulants, such as carbaminoylcholine, is probably beneficial in the majority of cases in which the condition is persistent.

Osteitis Deformans.—O'Farrell [34] emphasizes the value of the determination of the phosphatase content of the blood in the diagnosis of osteitis deformans. If the normal value for the adult is taken to be 4 units, in cases of Paget's disease the value has occasionally been as much as 130 units. Osteoplastic skeletal metastasis, especially when secondary to prostatic carcinoma, is the only disease of the bone in which such high figures are obtained. In cases of osteitis fibrosa cystica the phosphatase content is seldom above 10 units.

Interosseous Muscles of the Hand.—Salisbury [35] studied the interosseous muscles in 30 hands in order to refute the frequently accepted

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31. Fehr. A.: Beitr. z. klin. Chir. **165**:88, 1937.

32. Bissell, A. D., and Brunschwig, A.: Squamous Epithelial Bone Cysts of Terminal Phalanx and Benign Subungual Squamous Epithelial Tumor of the Finger, J. A. M. A. **108**:1702 (May 15) 1937.

33. Middleton, D. S.: Glasgow M. J. **9**:115, 1937.

34. O'Farrell, P. T.: Irish J. M. Sc., January 1937, p. 1.

35. Salisbury, C. R.: J. Anat. **71**:395, 1937.

statement that these muscles are inserted into the base of the proximal and the digital extensor expansion. He finds that the palmar interosseous muscles are inserted, with few exceptions, wholly into the extensor expansion. The first dorsal interosseous muscle is inserted wholly into the proximal phalanx. The other dorsal interosseous muscles are usually inserted into the bases of the proximal phalanges and the expansion, but usually by separate insertions arising from functionally separate portions of the muscle. The separation may be so complete as to form an extrapalmar interosseous muscle. The second dorsal interosseous muscle has a more complete insertion into the proximal phalanx than the fourth, and the fourth more than the third.

Urinary Concretions After Skeletal Disease.—Gold [36] calls attention to the often reiterated statement that stones in the renal tract occur in association with abnormal mobilization and excretion of calcium. Thus, renal stones are frequently found in cases of hyperparathyroidism. Even after parathyroidectomy has brought the calcium metabolism back to normal, death from uremia has been observed. The author reports that renal calculi will form in cases of skeletal metastases from mammary carcinoma and multiple myeloma. It is also known that stones will form after an overdose of vitamin D. The formation of renal stones after transverse myelitis is probably due to the associated renal infection.

ORTHOPEDIC OPERATIONS

Arthroplasty of the Knee.—Arthroplasty of the knee was performed on 5 patients by Mocquot and his co-workers.[37] Four of the patients were adults, and 1 was a child of 14 years. In 4 the ankylosis was fibrous and in 1 it was osseous. The condition in all followed acute infectious arthritis, either gonorrheal or pneumococcic. The technic of Putti was used. Postoperative continuous traction with a Kirchner wire was applied. Good functional results were obtained in all. The youngest patient had the least satisfactory result, motion being between 170 and 115 degrees. All were followed for four years or longer.

Arthrodesis of the Knee.—Key [38] describes a method of securing arthrodesis of the knee joint by the use of a large bone peg obtained from the tibial crest. The joint surfaces of the tibia and femur are cut off squarely as in the usual arthrodesis. Cavities extending into the bone are curetted and filled with bone chips. The bone peg, about 4 inches (10 cm.) long and ½ inch (1.3 cm.) thick, is removed from the tibia and driven into the femur. The hole is prepared in the upper end of the tibia with an osteotome, and the peg is shaped into this. The

36. Gold, E.: Wien. klin. Wchnschr. **59**:70, 1937.
37. Mocquot; Boppe, M., and Courvoisier: Rev. d'orthop. **24**:105, 1937.
38. Key, J. A.: South. M. J. **30**:574, 1937.

author has not used this operation on children for fear of damaging the epiphyses. He has found this method particularly satisfactory for the treatment of Charcot's arthropathy of the knee.

Arthrodesis of the Wrist.—The indications for arthrodesis of the wrist are, according to Logròscino,[39] tuberculous osseous lesions, a painful wrist due to arthritis, flaccid paralysis of the extensor muscles and similar conditions. The technic recommended consists of the following procedures: dorsal longitudinal incision of the wrist, separation of the tendons and exposure of the distal 8 cm. of the radius and proximal ends of the second, third and fourth metacarpals and insertion of a graft from 6 to 8 cm. long, obtained with a motor saw from the dorsal third of the radius, under bone flaps raised from the proximal ends of the second, third and fourth metacarpals. The proximal end of the graft is sutured to the radius proper, and the wound is then closed with the wrist in from 30 to 40 degrees of dorsiflexion. The accompanying roentgenograms show satisfactory fusion of the graft, which actually spans the wrist joint.

[ED. NOTE.—This procedure is relatively simple but has the fault of most types of purely extra-articular fusion in that the entire strain thrown on the wrist joint subsequent to operation must be borne by the graft.]

Operative Cure for Ingrown Toe-Nail.—Bartlett[40] divides operations for the treatment of ingrown toe-nail into two classes: (1) those which remove a strip of nail and matrix and (2) those in which the wall of the nail is made the site of plastic procedures. Because of the frequency of recurrence and prolonged disability from the usual operative procedures, the author reports a new method of treatment. This consists in the removal of a wedge of tissue from the lateral side of the foot from the base of the nail to a point midway between the tip of the toe and the corner of the nail. The wedge of tissue is ¼ inch wide at the edge of the skin and extends to the bone. When the edges of the skin are approximated, the wall of the nail is pulled away from the nail. The patient walks on the foot after twenty-four hours. The author has had no recurrences of ingrown toe-nail after this operation. Proper shoes are also essential for cure.

FRACTURES AND DISLOCATIONS

Fracture-Dislocation of the Cervical Vertebrae.—Cone and Turner[41] point out that fracture-dislocation of the cervical vertebrae is easily

39. Logròscino, D.: Chir. d. org. di movimento **22**:437, 1937.

40. Bartlett, R. W.: Conservative Operation for Cure of So-Called Ingrown Toenail, J. A. M. A. **108**:1257 (April 10) 1937.

41. Cone, W., and Turner, W. G.: J. Bone & Joint Surg. **19**:584, 1937.

reduced by prompt and appropriate treatment, but reduction can be maintained by a plaster jacket or some other kind of supporting jacket for a time only. When the jacket is removed, deformity may develop shortly after the support is taken away, or the deformity may gradually increase over a period of years until more energetic therapy is provided. In the past four years the authors have obtained fusion in 12 of the 36 patients with injuries to the cervical vertebral column. They feel that satisfactory end-results have been obtained by fusion. Six cases are reported in detail, 3 of fracture-dislocation in the upper cervical region and 3 of fracture-dislocation below the third cervical vertebra. Skeletal traction is applied to the cervical portion of the spine by means of tongs or heavy rustless steel wire through small openings in the skull. This apparatus can be quickly attached to the bed, and a vertical screw arrangement permits the angle of traction to be altered slowly and smoothly. By altering a notch arrangement at the head of the bed, the angle of traction can be changed in order to facilitate reduction. During operation, traction is maintained. Curved bone grafts obtained from a rib or from the ilium are held in place with rustless steel wire. As soon as the wounds permit, fixation of the head, neck and torso is maintained in a plaster cast, and the skeletal traction is removed. Immobilization in a plaster cast should be maintained for six months. When deformities recur after reduction in spite of careful immobilization, fusion is imperative. Another indication for fusion of lesions high in the cervical portion of the spine is paralysis of the muscles of the neck due to cellular involvement of the anterior horn. Fusion immediately protects the patient from recurrence of deformity. In occipitocervical fusion, rotation is lost, but considerable compensatory flexion remains. In this series of cases the patients resumed their previous occupations. The follow-up periods range from nine months to four years. The ages of the patients range from 6 to 72 years. No deaths and no infections of the wound were reported.

Fracture-Dislocation of the Cervical Portion of the Spine.—Roberts [42] reviews the treatment of fractures and dislocations of the cervical portion of the spine, basing his conclusions on 37 patients seen at the Massachusetts General Hospital. Early treatment of such fractures consists of traction with the neck in hyperextension. After reduction, a plaster cast is applied which extends from the top of the head to the pelvis, so that motion in the cervical portion of the spine is prevented. In Roberts' series of patients there were 4 with fracture of the spinous process. Treatment consisted of traction and later fixation in hyper-

42. Roberts, S. M.: J. Bone & Joint Surg. **19**:199 and 477, 1937.

extension. Nonunion without symptoms resulted in 1 patient. There were 5 patients with fracture of the odontoid process. Fixation was maintained for six months. Nonunion without symptoms resulted in 1 patient, and there was 1 death. Twelve patients suffered from fracture of the vertebral body; in six the sixth cervical vertebra was involved. Treatment consisted of hyperextension and traction with an inflated pillow under the shoulders, which was gradually raised until reduction was accomplished. Two patients showed permanent irritation of the nerve root. Nine patients, or 75 per cent, of the patients with fracture showed symptoms due to compression of the cord. In 5 of these damage to the spinal cord was permanent, and death resulted. There were 19 patients with dislocation of cervical vertebrae; only 7 had symptoms referable to the nerves. One death occurred in this group. Operative reduction was attempted on these 19 patients. Open operation is rarely necessary. Treatment for this type of injury consists of immediate reduction and fixation in a plaster cast. For incomplete dislocation, hyperextension and traction alone are sufficient. With the patient under general anesthesia and in the supine position, traction is applied by means of a band of cloth which is passed under the chin and occiput of the patient and is then attached about the waist of the operator. By gentle manipulation, after the method of Walton, the dislocation is reduced. Fixation is maintained for eight weeks, after which exercises are given.

Fracture of the Pelvis.—Rankin [43] reviews the results in 449 fractures of the pelvis treated in four hospitals in Philadelphia from 1907 to 1934. The ages of the patients varied from 1 to 80 years. Sixty-two per cent of the fractures were in males. Thirty-six per cent were due to injuries from automobiles. The fractures of the pelvis tended to be multiple; the ilium and the superior ramus of the pelvis were fractured most commonly. The treatment of choice was suspension in a hammock, with traction on the lower extremities. Treatment varied from simple rest to operative procedures. Seven operations were performed for internal injuries. One hundred and forty-four patients were discharged as well, 249 as improved and 4 as unimproved; 11 were released against advice, and 41 died. Twenty patients died during the first twenty-four hours. Four patients died of shock, 4 of pulmonary edema, 3 of internal injuries and 2 of a ruptured bladder. Only 3 per cent of the patients had severe injuries to the bladder. The other chief disability subsequent to injury was pain in the back or legs. Sixty-seven per cent stated that they were cured six months after injury; 25 per cent had shortening of a leg, which could have been

43. Rankin, L. M.: Ann. Surg. **106**:161, 1937.

prevented by traction. The average period of total disability in the uncomplicated cases was sixteen and four-tenths weeks. The author advises the early use of physical therapy in treatment.

Conservative Treatment of Fractures of the Leg.—Deuticke and Martys [44] report on 1,070 fractures of the legs treated from 1923 to 1934. Seven hundred and ninety of the fractures involved both bones; 211 of these were compound fractures. There were 109 isolated tibial fractures, 13 of which were compound. One hundred and seventy-one of the fractures included those of children and subperiosteal fractures. The mortality for adults was 2.5 per cent; that in the cases of closed fracture was 1.1 per cent, and in the cases of compound fracture, 6.8 per cent. The authors prefer manual reposition and fixation in an unpadded cast whenever possible. Anatomic reposition went hand in hand with the excellence of the final result. Various complications resulted in the patients (506) treated by extension. Infection developed in 6, necessitating removal of the bone clamps; the infection cleared up in 5 on removal of the clamps, but in 1 incision was necessary. Two patients died of sepsis, possibly due to the use of the clamps. Pulmonary embolism occurred in 4 cases of closed fracture during extension, mostly at the end of the second week of extension. Infarcts of the lungs, which did not prove fatal, occurred in 6 cases during extension. In general, extension delayed union and appeared to increase the chance of pseudarthrosis. It also decreased motion in the joint a trifle. Of 275 patients on whom a bone clamp was used 15 complained of painful scars at the site. While extension is often indispensable, it should be avoided wherever possible. Of 285 cases of closed fracture pseudarthrosis occurred in 1, while of 90 cases of compound fracture, pseudarthrosis occurred in 5. The femur was amputated in only 1 of 375 cases of fracture of both bones of the leg. In 62 per cent of the cases complete normal function and structure were obtained.

End-Results in Injuries to Epiphyses.—One hundred and six patients with traumatically displaced epiphyses were observed by Lipschultz [45] during a period ranging from sixteen months to eight years after injury. Only a small percentage of these patients were seen less than two years later. This time interval is considered sufficiently long for disturbances of growth to manifest themselves if they are to take place at all. In 15 cases there was roentgenographic evidence of premature ossification and suppression of growth. This group is made up of 6 cases of dislocation of the epiphysis of the radius in which there was retarded growth ranging from 6 to 16 mm., 3 cases in which the epiphyses for the medial epicondyle of the humerus failed to unite after separa-

44. Deuticke, P., and Martys, F.: Arch. f. orthop. u. Unfall-Chir. **38**:54, 1937.
45. Lipschultz, O.: Radiology **28**:223, 1937.

tion, 3 cases in which there was premature ossification with shortening of the ulna, 2 cases in which the proximal epiphysis of the humerus was involved in a similar manner and 1 case in which the separated epiphysis for the lesser trochanter of the femur united, with deformity. In only 3 of these many cases was there noted a light disturbance in function; in these 3 there was separation of the epiphysis of the medial epicondyle of the humerus with nonunion and as a result slight limitation of extension. In all the other cases there was no limitation of motion. The authors conclude that premature ossification with changes in growth takes place frequently after injury to the epiphysis. This condition was found 15 times in the series of 106 cases, or an incidence of 14 per cent, but the amount of shortening was usually minimal and not of clinical significance. Occasionally, however, a case is seen in which the disturbance in growth is marked, resulting in deformity and disturbance of function. This occurs whether or not perfect reduction is obtained and is apparently due to trauma to the epiphysis itself at time of injury.

Isolated Fracture of the First Rib.—Betto [46] reports a case of bilateral symmetrical isolated fracture of the first rib. Reports of 2 similar cases were found in the literature. The mechanism of these fractures is discussed at great length. A unilateral fracture of the first rib may follow a severe injury or a blow on the clavicle. On the other hand, Betto believes that bilateral fracture of the first rib occurs when a severe blow or force is applied to the sternum at the moment the scalenus anticus muscles contract violently. In the case reported the injury occurred in an automobile accident, and there was evidence of contusion of the sternum. An associated tear of the pleura with emphysema of the soft tissue has been reported. Therapy consisted in immobilization by strapping to limit respiratory excursion.

Recurrent Dislocation of the Shoulder.—Stefanini [47] describes a method of treatment for recurrent dislocation of the shoulder which has been used in 36 cases, with excellent results in all. The operative technic is as follows: The patient is supine with the arm in abduction. The incision follows the anterior border of the deltoid muscle from the clavicle to the midarm. The greater tuberosity of the humerus is exposed, and a piece of bone is removed to serve as a graft. The coracoid process is then exposed. The fibers of the coracobrachialis muscle are divided, and a bed is made for the graft. The graft is fixed in place with a catgut suture, and the fibers of the muscle are reunited. The wound is closed, and the arm is immobilized in a sling for ten days, after which use is slowly begun.

46. Betto, O.: Chir. d. org. di movimento **22**:424, 1937.

47. Stefanini, J.: Rev. de chir., Paris **56**:393, 1937.

Hanging Cast for Fracture of the Humerus.—LaFerté and Rosenbaum [48] used the hanging cast in the treatment of fractures of the shaft and neck of the humerus in 58 cases. No comminuted fractures of the head of the femur or fractures involving the condyles were treated by this method. The treatment consists of reduction of the fracture, after which a plaster is applied from the upper third of the humerus to the hand with the elbow at right angles. A plaster wedge is applied to the inner side of the cast just above the elbow to prevent angulation. The cast is carried in a sling. Motion in this at the shoulder and wrist is encouraged. In the cases in which the authors used this method delayed union or nonunion was not observed, and no bad results were encountered. Physical therapy to recover muscular function was necessary in only 20 of the 58 cases. The casts were removed in from five to eight weeks. This type of therapy was first described by Caldwell.[49]

Fracture of the Radius.—Since 1928 the Boehler method of treatment has been used in a total of 873 cases of fracture of the radius at the wrist at Denk's clinic in Vienna.[50] This method consists of reposition with the patient under anesthesia and fixation in an unpadded plaster cast. Certain modifications of this method are practiced; noteworthy is delayed reduction of most fractures. Unless marked displacement is present, the fracture is kept splinted for at least twenty-four hours before reduction is performed. The delay permits swelling to reach a maximum before the cast is applied, according to the authors. The patient is carefully watched for circulatory disturbances. (In 1 of 2 early cases in which the splint was not properly applied, palsy of the ulnar nerve developed, which remained permanently.) In 85 of the cases in the reported series the plaster had to be split. The cast is left for from three to five weeks, union and painless function in the cast comprising the indications for removal. Nonunion of the ulnar styloid process resulted in 152 of 248 cases. Dorsal subluxation of the ulna was observed in 26 and volar subluxation in 9 of the cases in which reexamination was made. The authors agree with others that longer fixation in a long arm plaster cast is indicated but are skeptical about 100 per cent good results. As to results otherwise, good cosmetic and functional results were obtained, if there existed no tendency to axial shifting. When a tendency to shortening of the radius appeared, good function and a poor cosmetic result were obtained. While ideal anatomic reposition is aimed at, it is not an absolute neces-

48. LaFerté, A. D., and Rosenbaum, M. G.: Surg., Gynec. & Obst. **65**:231, 1937.

49. Caldwell, J. A.: Ann. Surg. **97**:161, 1933.

50. Kotrnetz, H., and Geiringer, F.: Arch. f. Orthop. u. Unfall-Chir. **37**: 504, 1937.

sity for a good functional result. On the contrary, excellent repositions, as shown roentgenographically, were not always associated with corresponding function. Attempts at reposition after from eight to fourteen days delay healing about two weeks and tend to increase circulatory disturbances. Seven types of fractures about the wrist are listed. The severe intra-articular fractures healed, in general, in twelve weeks, while the transverse fractures healed in from seven to nine weeks.

Pseudarthrosis of the Scaphoid Bone of the Hand.—Boerema,[51] of Holland, reports on a group of 36 fractures of the scaphoid bone of the hand. Six of these were old fractures, removal of the ulnar fragment having been done more than ten years before. About half of the fractures (the early ones) had been treated by mobilization. The remaining half (recent fractures) were treated by immobilization in ulnar abduction, according to the method of Boehler. Of 17 patients in whom pseudarthrosis developed, 15 had limitation of volar and especially of dorsal flexion up to 50 per cent of normal. Two had normal range. Seven of the patients were obliged to seek a less arduous occupation because of pain. Two, despite pseudarthrosis, suffered in no way as far as work was concerned. Limitation of motion bore no relation to disability for labor. In short, objective signs were no measure for subjective complaints. The author takes issue with Boehler's absolutely favorable prognosis in this fracture. (Boehler reported 100 per cent union in 150 cases of recent fracture.) However, Boerema is in favor of this type of treatment. He reports spontaneous union in 5 cases without treatment of any sort and reproduces roentgenograms. In 3 of these cases the fractures were incomplete. Of the 6 patients operated on by removal of the ulnar fragment prior to the development of arthritic changes, all but 1 were able to resume full use of the hand, a matter of much surprise to the examiner.

Mallet Finger.—Smillie[52] reports a series of 35 consecutive cases of mallet finger. In recent cases fixation in a plaster of paris cast is employed. A 2 foot (61 cm.) length of dry starched crinoline is rolled into a tube of approximately the same size as the injured finger. One end of the tube is cut on a slant, so that it will fit closely at the web. The tube is slipped over the finger, and the finger and tube are dipped into water. The patient holds the terminal joint in hyperextension and the proximal interphalangeal joint in flexion by pressing the front of the distal end of the finger against the thumb until the plaster dries. The plaster is kept on for at least five weeks. In cases of long standing the ruptured tendon is brought into position and the finger is fixed as before, a sterile plaster bandage and sterile water being used.

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51. Boerema, I.: Arch. f. orthop. u. Unfall-Chir. **38**:42, 1937.
52. Smillie, I. S.: Brit. J. Surg. **24**:439, 1937.

Conservative Therapy for Fracture of the Os Calcis.—Hermann [53] is particularly concerned with that type of fracture of the os calcis in which there is a rather formless comminution of the bone as a whole, with a lateral broadening and pushing up of the posterior part of the heel. The results of treatment in 152 cases of fracture of the os calcis seen in the orthopedic service at the Boston City Hospital are presented. Preliminary treatment consists of the taking of roentgenograms, lateral and axial views of both heels being taken. The film of the uninjured heel is used for a comparison with the measurement of the injured heel and also to detect any bony anomalies. Since in about 10 per cent of the cases fracture of the spine occurs as well, routine roentgenograms of the lower lumbar and thoracic portions of the spine are also taken. The emergency treatment consists of encasing the foot comfortably in a "pillow and sides splint," with appropriate bleb dressing and the use of an ice bag if deemed necessary. A two day preparation of the bone is carried out as soon as the acute local reaction has subsided. This may require from one to ten days. For reduction and fixation, an operating kit is necessary which contains a tightly rolled sterile towel, a sand-bag, a 7 pound (3 Kg.) wooden mallet, a pair of bone tongs and a Forrester bone clamp, a sawed-off crutch, a scapel, sterile dressings and two rolled pieces of silk, 4 by 1¼ inches (10 by 3.2 cm.) in size. The technic is as follows: General or spinal anesthesia is used, and with the patient turned on the side opposite the injury a sand-bag is placed under the inner side of the heel. A tightly rolled towel is placed beneath the external malleolus and with solid blows the piled up bone beneath the external malleolus is pounded down until the normal depression between the external malleolus is restored. Next, with the scapel small stab wounds are made in the upper posterior part of the heel, and the tongs are driven in and locked. The crutch is used for countertraction, the handle resting against the operator's abdomen or chest and the cross bar of the sawed off portion resting against the sole of the foot in the line of the calcaniocuboid and the astragaloscaphoid joints. Traction is maintained by means of the tongs to overcome the pull of the muscles of the calf. The tongs are then removed, and the heel is remolded by the use of the Forrester bone clamp. When the desired compression has been obtained, traction is again applied through this clamp. The entire heel is carefully molded in this fashion. Roentgenograms are taken. The tongs are removed and a low plaster of paris cast is applied with the foot in slight inversion and in extreme plantar flexion. While the cast is hardening, manual pressure is applied over the pads beneath the malleoli. The first cast is removed in two weeks. The malleolar pads are then carefully replaced, and with the foot at right angles a new cast is applied.

53. Hermann, O.: J. Bone & Joint Surg. **19**:709, 1937.

This is repeated every two weeks for from ten to twelve weeks in order to maintain constant pressure beneath the malleoli, which retards callus formation. After removal of the last cast, a special ambulatory splint is applied at once. Physical therapy is then instituted. Full weight bearing without crutches but with the ambulatory splint is begun ten days or two weeks after omission of the last cast. Six weeks later, or four and one-half months after the initial reduction, the ambulatory splint is removed. If the patient complains of persistent pain in the region of the subastragalar joint and the original fracture was of the interarticular type and comminuted, then and only then is fusion of the subastragalar joint considered. The results in the 152 cases studied have been divided into good, fair and poor. Good results were obtained in 111 cases, or 75 per cent; fair results in 21 cases, or 14 per cent, and poor results in 20 cases, or 13 per cent. The patients with good results were those who by the sixth or seventh month had regained full functional use of the injured heel and had no pain or discomfort in any part of the heel after normal activity.

Treatment of Pseudarthrosis; Result of Ten Years' Experience.—In a statistical report on 181 cases of pseudarthrosis of the long bones in which operation was performed, Pfab [54] notes that healing occurred in 157 and that it had not taken place in 24. Various methods were employed (drilling, step formation with bone fixation, sliding bone grafts with fixation with kangaroo tendons and wire). Pseudarthrosis developed in 69, or 9.4 per cent, of 7,296 cases of fracture seen over a ten year period. Twenty-three of the author's 69 personal cases of pseudarthrosis occurred in a total of 400 cases of open fracture, while 46 occurred in a total of 6,896 cases of closed fracture.

Planes of Displacement and Zones of Destruction in Fractures.—Haase [55] reports another case of "gradual fracture," this time of the clavicle in a 47 year old worker, and attributes it to the fatigue of bone. Just as the structure of inanimate materials are injured by overloading, tensions and strains, so the structure of bone undergoes changes when its physical characteristics are insufficient to resist the stresses applied. When an aluminum strap is pulled apart, the tear is at an angle of 45 degrees to the axis of pull, and stress lines appear at right angles to the tear as well. When bone or wood blocks are subjected to compression, oblique fracture planes occur at an angle of about 45 degrees to the long axis of compression. Also, distant changes occur in the physical structure apart from the immediate zone of fracture. Even when not directly visible, injuries to the capillary structure of bone must accompany these distant changes. These disturbances may later make

54. Pfab, B.: Arch. f. orthop. u. Unfall-Chir. **38**:90, 1937.

55. Haase, W.: Arch. f. orthop. u. Unfall-Chir. **37**:592, 1937.

their appearance clinically. Close roentgenographic study of the shafts distant from the site of fracture will occasionally give evidence of such damage.

The Effect of the Electrolysis of Metals on the Bone.—Venable and his co-workers,[56] after a study of the electrolysis of various metals in the tissues, came to the following conclusions: It is impossible from macroscopic, microscopic and roentgenographic studies to determine the reactions of soft tissues and bone to metals. Electrical force is generated when different metals are placed in tissues, the amount of electric current produced being dependent on the difference in potential of the metals and the distance between the poles. Pure metals alone are inert. Any reaction about them is wholly chemical. Any appliance of galvanized iron, plated steel or metallic alloy causes some galvanic action. In the selection of alloys, those containing iron show the greatest reaction. Chromium is readily liberated on plating and is very toxic. The authors suggest that an alloy similar to vitalium in which vanadium may be substituted for the chromium be used for bone work.

Serum Phosphatase in Diseases of Bone.—Mitchell and Crawford[57] review the literature pertaining to the clinical application of serum phosphatase to diseases of the bone and, in addition, present an analysis of the readings taken in several hundred cases of osseous lesions. Their results show that in general there is an increase in activity of the serum phosphatase accompanying the formation of unusual amounts of new or of abnormal bone. There appears to be little or no increase associated with the purely destructive lesion of bone. Determinations of serum phosphatase are important aids in the diagnosis and differential diagnosis of Paget's disease, osteitis fibrosa cystica and tumors of bone. The level of the activity of the serum phosphatase cannot be used as an index of healing or of the ability of a fracture to heal. No significant changes in the activity of serum phosphatase were noted in cases of tuberculosis of the bones and joints and of osteomyelitis. Determinations of the serum phosphatase are suggested as a criterion of effective therapy in Paget's disease, hyperparathyroidism, osteoblastic osteogenic sarcoma and rickets.

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56. Venable, C. S.; Stuck, W. G., and Beach, A.: Ann. Surg. **105**:917, 1937.
57. Mitchell, C. L., and Crawford, R. R.: J. Bone & Joint Surg. **19**:630, 1937.

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